One-stage repair of complete unilateral cleft lip and palate

Dentofacial treatment outcome

Piotr Stanislaw Fudalej

Piotr Stanislaw Fudalej

One-stage repair of complete unilateral cleft lip and palate Dentofacial treatment outcome

Thesis Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands
ISBN ………………….

Cover design and printed by: Benda Drukkers, Wijchen, The Netherlands

One-stage repair of complete unilateral cleft lip and palate

Dentofacial treatment outcome

Een wetenschappelijke proeve op het gebied van de Medische Wetenschappen

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. mr. S.C.J.J. Kortmann
volgens besluit van het college van decanen
in het openbaar te verdedigen
op woensdag 8 juni 2011 om 10.30 uur precies

door

Piotr Stanislaw Fudalej
geboren op 14 januari 1968
te Sosnowiec, Polen

Promotor:
Prof. dr. A.M. Kuijpers-Jagtman

Manuscriptcommissie:
Prof. dr. P.H. Spauwen (Voorzitter)
Prof. dr. A. Verdonck (Leuven)
Dr. W.A. Borstlap

Paranimfen:
Dr. R.M.M.A. Kiekens
Dr. M.A.R. Kuijpers

The study presented in this thesis was conducted at the department of Orthodontics and Craniofacial Biology (Head: Prof. dr. A.M. Kuijpers-Jagtman), College of Dental Science, Radboud University Medical Centre Nijmegen, the Netherlands.
This research is part of the research institute NCEBP / Nijmegen Centre for Evidence Based Practice

NCEBP
science for care,
care for science

To my wife, Sylwia and my children:
Maja, Pola, Marek, Tomek, and Jacek.

Table of contents

Chapter 1

General introduction

1.1 Etiology and epidemiology of the cleft deformity

Orofacial clefts are among the most common human congenital malformations, second only to heart defects. They develop between the 4^{th} and 10^{th} week post conception due to a partial or complete lack of fusion of the maxillary prominence with the medial nasal prominence on one or both sides into clefts of the lip, alveolus and anterior palate or due to a lack of fusion of the palatine shelves into clefts of the palate posterior to the incisive foramen.[1] Although unique causal factors remain unknown, presently it is widely accepted that orofacial clefts are of multifactorial etiology, with genetic predisposition and environmental influence playing a role.[2] While no strong risk factors have been identified, maternal cigarette smoking,[3] alcohol consumption,[4-6] anti-epileptic drugs,[7,8] or corticosteroids administered topically or systematically[9] are among few of them showing an association with increased incidence of various subtypes of clefts. Inadequate maternal nutrition during pregnancy, and related with it, lower socioeconomic status, have also been suspected as conducive to occurrence of oral clefts.[10,11] Influence of a genetic defect is obvious in some syndromic forms of orofacial clefts. For example, in the van der Woude syndrome that manifests with cleft lip and/or palate and lower lip pits, a deletion in chromosome 1q32-q41 or in a second chromosomal locus at 1p34 has been linked to disturbance of the interferon regulatory factor-6 (IRF-6) gene, but the exact mechanism of influence of this mutation on craniofacial development is uncertain.[12] In non-syndromic clefts, however, the understanding of multi-gene and gene-environmental interactions in the development of the cleft is incomplete.[13] Although investigations of familial occurrence of clefts or twin studies emphasized a relationship between genetic makeup and cleft anomaly,[14] more research is needed to pinpoint genetic markers of the oral cleft.

Regardless of the underlying mechanism or cause of the clefting malformation, orofacial clefts demonstrate a great heterogeneity as to severity, prognosis, or concurrence with other syndromes. According to the classification system proposed by Kernahan and Stark[15] orofacial clefts are categorized as clefts of the primary palate (cleft of the lip, alveolus and anterior part of the hard palate extending to the incisive foramen), clefts of the secondary palate (cleft of hard and soft palate, extending from the incisive foramen to the uvula), or combined forms where the cleft deformity involves both the primary and secondary palate. However, based on embryology, it is common to report on combined clefts of the lip with or without clefts of the palate (CL/P) as opposed to isolated forms of cleft palate (CP) since they do not share a common inheritance pattern.

Average worldwide prevalence of all facial clefts is approximately 1.7 per 1000 live births,[16] but considerable differences exist for individual subtypes in various ethnic and racial groups, geographical locations, or genders.[13] Among populations with the highest reported prevalence of CL/P are Native Americans, with 3.6 cases per 1000 live births, Asians who demonstrate 2.1 cases of CL/P per 1000 Japanese live births or 1.7 cases of CL/P per 1000 Chinese live births.[17] Also in relatively homogenous Europe there is an apparent correlation between frequency of orofacial clefts and geographical latitude.[13] The areas with the highest prevalence of CL/P are the Scandinavian countries and the lowest prevalence is noted in southern Europe. Intermediate levels occur in the central part of Europe.[13,16] Data from the U.S. revealed a correlation with geographical longitude, i.e. an increasing frequency from East to West in North America. The incidence of cleft palate (CP) is much less dependent on racial and ethnic factors, being approximately 0.5 per 1000 live births.[18]

The strict registration system of orofacial clefts that was introduced in Denmark in 1936 allowed to examine changes in oral cleft frequency over time.[14] From 1936 to 1961 a steady increase in the prevalence of both CL/P and CP was observed followed by a fairly constant frequency of incidence of orofacial clefts from 1962 to 1987. It was suggested that an improvement of survival of new-born CL/P cases and a better ascertainment during the first observation period, especially of milder forms of CP, could explain the increased prevalence in the first observation period.

Polish epidemiological data show the incidence of all orofacial clefts at approximately 2.0 per 1000 of live births in Lódź from 1981 to

1995[19,20] and 1.67 per 1000 in the district of Lódź from 1996 to 2000.[21,22] Fogh-Andersen[23] using Danish data, reported a cleft lip (CL):cleft lip and palate (CLP):cleft palate (CP) ratio of 1:2:1, which is often used as the normal proportion for cleft subtypes in most European populations. However, in the Polish population this ratio differed from that presented by Fogh-Andersen due to a relatively higher incidence of isolated CP and lower incidence of CLP resulting in a ratio 1:1.55:1.3.[22]

Studies of Caucasian populations revealed that CL/P occurs more frequently in boys than in girls, with an average male to female ratio of 2:1.[24] Conversely, females demonstrate a slightly higher incidence of isolated CP than males.[24] Unilateral clefts form 80–85% of all CL/P cases.[25,26] Two-thirds of the unilateral clefts are left-sided regardless of sex and severity of the defect.[25,27]

1.2 Treatment outcome and timing of cleft repair

The specific location of the cleft anomaly leads to impairment of basic life functions of the infant such as sucking, swallowing, breathing and, later, often speech and hearing. Despite prolonged multispecialty treatment, delivered usually by organized multidisciplinary teams, residual deformities and/or functional disturbances are frequently seen in adult patients with a repaired cleft. The extent of residual dentofacial deformities is various and depends on the cleft subtype. In a relatively homogenous category - unilateral cleft lip and palate (UCLP) – the resulting growth disturbances range from increased interocular width to a general retrusion of the midface relative to the cranial base involving the nasal bone, maxilla, and mandible. Both the maxilla and mandible are shorter and retrusive, and the incisors in both jaws are retroclined. The narrowed upper dental arch results in frequent posterior crossbites. The mandible has an increased gonial angle and a steeper mandibular plane in comparison to a noncleft population.[28] The pattern of growth is also different. Semb[29] detected almost no increase of the length of the maxilla from 5 to 18 years of age in subjects with UCLP. The distance from *subspinale to pterygomaxillare* increased by 1.4 mm in the UCLP group as opposed to 10 mm increase in the noncleft group.

An aberrant facial growth pattern as often found in CLP patients results from a combination of intrinsic growth deficiency, functional adaptations, and, above all, surgical iatrogenesis.[28] The detrimental effects of surgery are associated with formation of scar tissue. Numerous experiments demonstrated that denudation of the palatal bone followed by scarring plays a major role in maxillary growth inhibition. Kremenak et al.[30,31] investigated maxillary development in *beagle dogs* following asymmetrical denudation of the palatal bone. They observed that 62 weeks post-surgery the maxilla on the side where the mucoperiosteal flap had been removed and palatal bone was denuded, was constricted by 25%. Leenstra et al.[32] hypothesized that leaving the palatal bone covered with periosteum would result in better maxillary arch development. In an experimental set-up in *beagle dogs* they compared the dentoalveolar development after palatal repair according to the partially split flap technique and the von Langenbeck method. The use of a partially split flap technique resulted in significantly wider transverse dimensions of the maxillary dental arch than after the von Langenbeck procedure. Ishikawa et al.[33] investigated the relationship between maxillary dental arch form and distribution of postsurgical scar tissue in 21 Japanese patients with isolated cleft palate. The authors concluded that the severity of the maxillary dental arch constriction was closely related to distribution of scar tissue on the palates. Kim et al.[34] evaluated two components of transverse growth disturbance: inhibition of lateral growth of the basal maxilla and inclination of teeth after surgical denudation of the palate in rats. They noticed that bone denudation primarily resulted in an increased medial inclination of the teeth, whereas lateral growth of the palatal bones was less affected. Less maxillary growth disturbance was also shown in animal experimental studies, in which denuded palatal bones were covered with atelocollagen matrix[35] or free mucosa.[36] Fujioka and Fujii[35] implanted atelocollagen matrix - a factor preventing scar contraction - on the denuded bone in fifty 4-week-old rabbits and found that in adult rabbits the atelocollagen-applied scars showed less contraction, the area and width of atelocollagen-implanted palatal processes showed more satisfactory growth, and the dental arch deformity was less in comparison with the control side. Meng and co-authors[36] showed comparable findings in experiments where the denuded palate in 45 rabbits was covered with free buccal or palatal mucosal grafts showing that the mucosal graft might have prevented maxillary deformity.

Although growth inhibition after UCLP surgery may be the result of lip as well as palate repair - separation of the effects of lip closure from those of palate repair is difficult since the results of lip closure are overshadowed by the results of palate closure performed usually 6 to 18 months later - most strategies to minimize detrimental iatrogenic effects concern palatal surgery. Besides refinement of surgical techniques, a postponement of hard palate closure to allow undisturbed maxillary development is a frequent approach; it has become routine in approximately 25% European cleft centers.[37]

The theoretical possibility of two-staged palatal closure was first discussed by Gillies and Fry,[38] who believed that early repair of the soft palate would be advantageous for speech, and late closure of the hard palate would be beneficial for maxillary growth. In 1951 Schweckiendieck[39] published long-term results of his delayed hard palate closure *(DHPC)* approach and he reported very good facial growth in his sample. In a comprehensive review[40] of 538 male patients with UCLP collected from 15 cleft centers from around the world, 34 subjects treated by Schweckendieck were included, in whom the soft palate was closed in infancy, whereas the hard palate remained unrepaired until after puberty. In this group excellent, uninhibited growth of the maxilla in vertical and sagittal dimensions was found. Favorable growth outcomes were also reported by Hotz and Gnoinski,[41] Hotz,[42] Robertson and Jolleys,[43] and Chait et al.,[44] but Schweckendieck's standards of near normal growth have not been met. Friede, an exponent of the Gothenburg cleft center practicing DHPC since 1975, in a recently published review[45] concluded that ...*the average maxillary growth outcome of a DHPC protocol can be very good*....

However, more recently the possibility of unsatisfactory speech performance has become a main argument against DHPC. Cosman and

Falk[46] found that 68% of 32 children treated with DHPC failed to develop acceptable speech spontaneously. A very high percentage suffered nasal and a high proportion required pharyngeal flaps. Bardach et al.[47] found that 35 of 43 subjects (81%) from the sample treated by Schweckendieck showed velopharyngeal incompetence. Rohrich et al.[48] evaluated 44 postadolescent patients with early (at 10.8 months) versus late (at 48.6 months) closure of the hard palate and found greater speech deficiencies in DHPC group, especially in articulation, nasal resonance, intelligibility, and substitution pattern assessment. Likewise, the persistent palatal fistula rate in the late closure group was 35% in comparison with 5% for the early closure group. Holland et al.[50] compared two groups of 41 adults who underwent early one-stage palatal closure or *DHPC* and detected a lower fistula rate (11% vs. 58%) and better speech outcome in the group that had a one-stage palatal repair. These findings raise an important issue: are the additional burdens of treatment imposed by DHPC justified, even if the growth results are more favorable? With the possibility of worse speech performance and the need for obturation of the palatal defect for several years before repair, the slight growth improvements, which may be possible, could equally well be negated in value because of these other concerns.

One-stage simultaneous closure of complete UCLP, as opposed to multi-stage protocols including DHPC, offers simplicity of the treatment program by minimizing the number of primary surgeries. Provided that the long-term outcome of the one–stage approach is comparable with the best multi-stage protocols, it may be an interesting alternative due to reduced burden of care.

1.3 One-stage simultaneous repair of complete UCLP - overview

One-stage surgical repair of UCLP has not attracted much attention from researchers. Only 9 studies could be identified in literature that deal with this topic. Table 1 gives an overview of the studies and in table 2, outcome measures and findings are presented. One-stage repair of complete UCLP was first mentioned in a scientific journal in 1958 by the Brazilian surgeon Farina.[50]

Table 1 Characteristics of the studies evaluating one-stage surgical repair of UCLP.

Author(s), year	Country	Type of study	Type of cleft	N	Timing of closure	Control group(s)	N	Timing of closure
Farina, 1958[50]	Brazil	retrospective	UCLP	23	> 1 year	No	n/a	n/a
Davies, 1966[51]	Republic of South Africa	retrospective	UCLP	20	5-6 months	No	n/a	n/a
Kaplan et al., 1974[52]	Israel	retrospective	UCLP and BCLP	13	3-4 months	Mixed (CP+UCLP)	13	3 months (lip) and 10-12 months (palate)
Kaplan et al., 1980[53]	Israel	retrospective	UCLP and BCLP	28	4 months	Mixed (CP+UCLP)	13	3 months (lip) and 10-12 months (palate)
Kaplan et al., 1982[54]	Israel	retrospective	UCLP and BCLP	28	4 months	Mixed (CP+UCLP)	13	3 months (lip) and 10-12 months (palate)
Hönigmann, 1996[55]	Switzerland	retrospective	UCLP (24 subjects) and BCLP (11 subjects)	35	6 months	No	n/a	n/a
Corbo et al., 2005[56]	Belgium	retrospective	UCLP	11	3 months	UCLP and Non-cleft	10 (UCLP), 10 (Non-cleft)	3 months (soft palate) and 6 months (lip + hard palate) - Malek's procedure
Savaci et al., 2005[57]	Turkey	retrospective	UCLP	19	7 months	UCLP and Non-cleft	22 (UCLP), 27 (Non-cleft)	5 months (lip) and 15 months (palate)
De Mey et al., 2006[58]	Belgium	retrospective	UCLP	18	3 months	UCLP and Non-cleft	26 (UCLP), 40 (Non-cleft)	3 months (soft palate) and 6 months (lip + hard palate) - Malek's procedure

n/a = not applicable

Table 2 *Outcome measures and findings of the studies evaluating the one-stage closure of UCLP – cont.*

Author(s), year	Length of follow-up	Outcome measures	Findings / remarks
Farina, 1958[50]	?	?	presentation of a rationale for 1-stage closure
Davies, 1966[51]	unclear, but likely a few months	unclear; post-operation health status	presentation of a rationale for 1-stage closure; description of surgical techniques
Kaplan et al., 1974[52]	unclear, but approximately 1-2 years	unclear; some general observations regarding psychosocial effects of 1-stage closure on the family, maxillary growth and speech development were made; no description of outcome measures	presentation of a rationale for 1-stage closure
Kaplan et al., 1980[53]	8-10 years	unclear; general observations regarding psychosocial effects, maxillary growth, occlusal status, incidence of otitis, speech development, and economic aspects were made; no description of outcome measures	presentation of a rationale for 1-stage closure
Kaplan et al., 1982[54]	10 years	unclear; general observations regarding psychosocial effects, maxillary growth, occlusal status, incidence of otitis, speech development, and economic aspects were made; no description of outcome measures	presentation of a rationale for 1-stage closure
Hönigmann, 1996[55]	unclear, but likely a few months/1-2 years	speech development	description of a technique of operation
Corbo et al., 2005[56]	12 years	cephalometric assessment of maxillofacial growth	no difference between 1-stage and 2-stage groups; significant differences between cleft and noncleft children
Savaci et al., 2005[57]	7-8 years	cephalometric assessment of maxillofacial growth	maxillomandibular retrognathism, more open palatal planes, larger anterior facial heights, and decreased posterior facial heights relative to noncleft children; no significant difference between cleft groups
De Mey et al., 2006[58]	10 years	cephalometric assessment of maxillofacial growth, evaluation of otologic status and speech development	generally no difference between 1-stage and 2-stage groups regarding facial morphology and otological status; better speech intelligibility in 1-stage group

The author described the surgical technique and listed a decreased risk associated with general anesthesia, better healing of soft tissues, lower incidence of fistulae, and reduction of costs of hospitalization as the rationale for performing one-stage closure of the cleft. Farina also mentioned that no post-operative complications had been encountered; however, he did not present the long-term observations. In the following years several similar reports focusing on the description of the surgical technique and discussing the advantages of a one-stage repair were published.[51-55]

Davies,[51] based on the review of 20 operated patients, described his personal experience with the one-stage method. He claimed that *...the child is spared multiple procedures, multiple anesthetics and has a very much shortened stay in hospital.* Although Davies cautiously declared that preliminary reports might *do more harm than good because they stimulate enthusiasm often on false promises and exaggerated claims*, he was enthusiastic about the ease of operation and postoperative results. He announced a long-term follow-up, but, to the author's knowledge, it was never published.

Kaplan et al.[52-54] in a series of 3 short articles claimed that one-stage repair had a positive psychosocial effect on the mothers, who tended to show less over-protection or over-attention toward their children; maxillary growth was undisturbed and speech development was comparable as in the non-cleft children. They listed the reduced costs of hospitalization as the additional benefit of one-stage closure. The investigators concluded that …*in spite of the relative paucity of cases and short follow-up, we feel justified in continuing this treatment of combined cleft lip and palate cases as a routine*.

In a preliminary report of a one-stage *(all-in-one)* closure of cleft lip and palate during the first year of life Hönigmann[55] proposed that reconstruction of a normal anatomy as early as possible as the base for normalization of muscle function, reduction of stress associated with hospitalization, and minimization of treatment costs justified one-stage repair of complete UCLP. The author observed normal healing in all parts of the reconstructed palate. Speech development was found *encouraging*. However, no long-term data were demonstrated.

A more contemporary research methodology was employed in the studies evaluating the outcome of one-stage approach, published in 2005[56,57] and 2006.[58] Two studies[56,58] assessed the results achieved at the Brussels Reine Fabiola Children's Hospital. Corbo et al.[56] cephalometrically examined craniofacial morphology in 2 groups of preadolescent children subjected to one- or two-stage repair according to the Malek technique and compared them to non-cleft controls. In the first group, the lip, soft, and hard palate were closed simultaneously. In the second group the soft palate was closed at 3 months, and lip and hard palate were repaired at 6 months. Facial morphology in both cleft groups was comparable but different from non-cleft controls. De Mey et al.[58] evaluated treatment outcomes in 18 patients whose cleft was closed in one operation at 3 months of age. The outcomes from this group were compared to a group of 26 patients with UCLP operated by the Malek procedure. This was a historical control study: from 1981-1988 the Malek procedure was used for all patients. In 1988 the one-stage procedure was adopted for all patients. Facial growth was assessed cephalometrically. No significant difference in antero-posterior midfacial growth was found between the two cleft groups, but the one-stage procedure resulted in less downward inclination of the maxillary plane relative to the anterior cranial base compared to the cohort operated according to the Malek procedure. Early closure of the complete cleft did not have any significant benefit for the otological status or the occurrence of nasality; however, earlier intelligibility of speech was found in the one-stage group.

Savaci et al.[57] examined craniofacial morphology in two samples of Turkish 7-year-olds with complete UCLP, which were closed during one (one-stage group, 19 subjects) or two surgical sessions (two-stage group, 22 subjects). 27 noncleft children matched for age formed the control group. No differences were found between groups with UCLP. However, maxillomandibular retrognathism, a more open palatal plane, and larger anterior and decreased posterior facial heights were demonstrated in children with UCLP in comparison with non-cleft controls. Savaci et al. concluded that since one-stage repair and *conventional* two-stage repair had affected maxillofacial growth to the same degree, one-stage approach might offer several advantages, such as lower costs or lower risk of nosocomial infections due to shorter hospitalization periods.

Studies discussed above had, however, various shortcomings. Most importantly, their methodological design was weak because none of them was a prospective trial. Moreover, among other limitations were short observation period,[51,52,55] relatively small sample sizes,[51,52,56,58] inclusion of children with unilateral and bilateral clefts in the study group,[52,55] the use of a non-consecutive sample for comparison,[56,57] or inappropriate methodology of evaluation of the treatment outcome.[52-54] In several studies a short observation period of only a couple of months[51,55] allowed detection of only early postoperative complications such as formation of fistulae. The use of small study groups[51,52,56] decreased the power of the study to detect differences. Inclusion of both uni- and bilateral CLP into the examined group[55] additionally increased variability of the outcome, whereas inclusion of selected rather than consecutively treated children[56-58] increased the risk of selection bias. In consequence, formulation of meaningful inferences is difficult and burdened with potential error.

Moreover one should bear in mind that one-stage simultaneous repair of UCLP is not a single entity. As the two-stage approaches demonstrate differences regarding, for example, use of infant orthopedics, timing of operations or surgical techniques, the one-stage protocols employed in various centers worldwide also differed in regard of timings or surgical methods. The surgical protocol described by Davies[51] included lip repair by Z-plasty followed by primary bone-grafting and Wardill-Kilner palatoplasty. Kaplan et al.[52-54] employed a Le Mesurier or Millard type of lip closure and a classical von Langenbeck technique for palatal repair. Hönigmann[55] repaired the cleft lip with a modified Millard technique, whereas the palate was closed by means of the Wardill-Kilner method. In the protocol described by Savaci et al.[57] lip repair was performed according to the Millard's rotation-advancement technique. Hard palate closure was achieved with the Wardill-Kilner palatoplasty but in patients who were suitable for a vomerine flap, a two-layer palatoplasty was performed. Soft palate closure was performed with the intravelar veloplasty in three layers according to Kriens. In the study by Corbo et al.[56] and De Mey et al.[58] the lip was repaired using the Tennison triangular flap technique, whereas the palatal closure was achieved with the Malek procedure. Timings of surgeries were also variable and ranged from 3[52,56] to 9[59,60] months of age.

Due to the methodological design of the reviewed above studies one can make only cautious inferences that the one-stage closure of complete UCLP may not be burdened with postoperative complications that would eliminate it from the surgeon's repertoire, and the craniofacial morphology at preadolescence may show approximately the same degree of deviation from the norm as in the patients who underwent multi-stage repairs of the cleft deformity. Suggested advantages of the one-stage approach, such as early normalization of the disturbed muscle function, positive psychosocial effect on the parents, reduced stress for the child and the whole family, lower costs of hospitalization, or reduced risk of nosocomial infections, although plausible, have not been substantiated yet.

1.4 Warsaw approach - one-stage simultaneous repair of complete UCLP

The one-stage approach of treatment of UCLP has been used at the Warsaw Institute of Mother and Child (IMC) since the early 1980's.[61,62] It was developed in response to previously achieved unsatisfactory results, as a large proportion of patients treated in the 1970's demonstrated poor facial development and had speech deficiencies.[61] The method was based on the assumption that minimization of scarring is a key feature for optimal maxillofacial growth and speech development. In order to eliminate formation of scar tissue on the surface of the palatal bones, soft tissues were always attempted to be sutured tightly. The technique evolved over the years. During the initiation of the technique lip repair was performed with a Tennison-Randall technique and the palate was closed with the von Langenbeck's approach. The one-stage method was subsequently modified to further minimize denudation of palatal bones by using an extended vomer flap for cleft palate repair.

Since May 1993, when the last modification was introduced, all patients with UCLP were operated on by the same surgeon by means of the fully developed method: the infant was operated between the 6th and 12th month of age; the Tennison-Randall technique was used to repair the lip, an extended vomer flap and modified von Langenbeck's approach were used to close the palatal cleft.

Dudkiewicz, from the IMC, assessed the outcome of the one-stage method several times.[62,63] Although the results appeared promising, they have only historical value today due to the modifications of the surgical technique over the years. Kulewicz,[64] also from the IMC, evaluated cephalometrically children subjected to the same protocol as is assessed in this thesis, but the length of follow-up was short. Fudalej et al.[59,60] limited their examination to the cephalometric assessment of facial morphology. All the above studies were *within-center* investigations.

1.5 Evaluation of treatment outcome in UCLP

1.5.1 Single center studies

Single center reports of treatment of UCLP have been by far the most common form of presenting outcomes. Although they are valuable because they may demonstrate the relative success of the practiced protocol by permitting comparison with published reports of other cleft teams, there are difficulties in making such comparisons due to the presence of potential biases, particularly analysis bias and reporting bias.[65] Analysis bias arises when different researchers employ rating scales or measuring techniques differently. Avoiding this bias also may be difficult when the rater knows the source of each record assessed. Reporting bias occurs when the efforts to document unsuccessful and successful cases are not exactly equivalent. To minimize this bias consecutive rather than selected cases should be included into a sample. Another major concern in retrospective within-the-center studies is the possibility of sampling bias, for if two or more therapies were being used concurrently in a single center, selective allocation to treatment must be suspected.

1.5.2 Intercenter research

Intercenter comparative studies have several advantages over within-the-center research. Firstly, they are less susceptible to potential biases, especially analysis and reporting biases, than single center investigations, partly due to openness during research sessions. Secondly, intercenter comparisons usually comprise more patients than single center studies, which allow more powerful statistics and enhance more reliable conclusions. Moreover, an intercenter approach fosters collaborative spirit and facilitates joint working, such as the development of rating scales and the formulation of new research questions.

Methodological standards for intercenter investigations of the effectiveness of treatment of the cleft deformity were established by the Eurocleft Project and its successor the EUROCRAN study,[37] which was designed to minimize methodological deficiencies of retrospective single center investigations. Inclusion of consecutively treated patients, all primary surgeries performed in the center concerned, diagnosis of complete UCLP confirmed by extra-oral photographs, and blinded assessment were all intended to maximize objectivity of the comparisons. Various components of treatment outcome as well as organization of services, burden of care and patient's satisfaction were evaluated and, subsequently, general conclusions regarding treatment were presented. However, an important limitation of intercenter retrospective comparisons is that it does not allow identification of the sole elements of the treatment protocol responsible for the advantageous or disadvantageous outcome. For example, if two centers differ in the use of infant orthopedics and type of primary lip and palatal surgery, it is not possible to determine which of these procedures might be responsible for any difference in outcome between centers; similarly, a lack of intercenter difference is not tantamount to the conclusion that individual aspects of the treatment program are equivalent. The intercenter study design is therefore better suited to comparative clinical audit than identification of the elements of the treatment protocol influencing its outcome. Nevertheless the existence of significant disparities in treatment outcome provides a basis for speculating as to the possible cause, and intercenter studies should therefore motivate formulation of specific hypotheses for more detailed testing.[66]

The etiology of differences in treatment outcomes between centers may be explained by means of a randomized controlled clinical trial (RCT). In RCT, thanks to the random allocation of different interventions to subjects, both known and unknown confounding factors are evenly distributed between groups. As long as numbers of subjects are sufficient, this ensures that samples being compared differ only in the type of studied intervention. Although randomized controlled trials are recognized as the epitome of scientific validity, they are burdened with higher costs, shorter time frame of observation and a narrower range of patients.[67] The RCT's in the management of cleft lip and palate present also other challenges, such as multiple-site coordination, the length of follow-up, and due to its low incidence, the generation of samples of adequate size.

Therefore the choice of study design – retrospective observational intercenter comparison vs. randomized controlled clinical trial – depends on the research question. If the goal of the study is, for example, establishing which of two different timings of hard palate closure is more favorable, a RCT should be performed. If, however, the question to be answered is *Which of the protocols produces the best overall treatment outcome? or How does our treatment program perform in comparison with other programs?*, retrospective observational comparison seems appropriate.

1.6 Objectives of the thesis

Treatment of children with a complete UCLP is prolonged and comprehensive. The range of outcome is considerable and may be related to variations in sequence, timing, and surgical technique, the orthodontic and orthopedic approach, the organization of cleft care, as well as the skills and experience of the surgeon and other clinicians involved. This thesis focused on craniofacial and orthodontic outcome variables. The overall objective of this study was to evaluate outcome following one-stage simultaneous repair of the complete cleft in patients with UCLP.

The specific aims were:

- To evaluate craniofacial morphology of preadolescent children with UCLP treated with the one-stage method in comparison with non-cleft Polish control children
- To evaluate dental arch relationship of preadolescent children with UCLP treated with the one-stage method in comparison with a UCLP sample treated with a three-stage method, including delayed hard palate closure (DHPC), as practiced at the Nijmegen Cleft Palate Craniofacial Unit
- To evaluate dental arch relationship of preadolescent children with UCLP treated with the one-stage method in comparison with a UCLP sample treated with a two-stage method as practiced at the Oslo Cleft Center
- To evaluate nasolabial esthetics of preadolescent children with UCLP treated with the one-stage method in comparison with a sample treated with a three-stage method, including delayed hard palate closure (DHPC), as practiced at the Nijmegen Cleft Palate Craniofacial Unit

1.7 Overview of the thesis

This retrospective comparative study was performed on the basis of records of patients consecutively treated at the Warsaw Cleft Center in the Institute of Mother and Child, Warsaw, Poland from May 1993 to August 1996. All examined individuals had a complete unilateral cleft lip and palate (UCLP) repaired during one surgical session by a single experienced surgeon. Subjects with and without Simonart's bands were included into the sample. All children were born between May 1992 and January 1996.

Chapter 1 introduces the topic of cleft lip and palate and general aspects of treatment of the UCLP deformity and gives an overview of one-stage simultaneous repair of complete UCLP. Scientific methodology used in cleft research is briefly summarized.

In *Chapter 2*, facial morphology of children with UCLP was cephalometrically evaluated and compared with facial morphology of non-cleft children of the same ethnic background.

In *Chapter 3*, mandibular morphology and spatial position in children with UCLP was evaluated on the basis of cephalograms and compared with mandibular morphology in non-cleft children of the same ethnic background.

In *Chapter 4*, dental arch relationship was assessed with the GOSLON Yardstick. In this within-the–center evaluation the photographs of study models were used for scoring.

In *Chapter 5*, dental arch relationship was assessed in an international setting with the GOSLON Yardstick and, subsequently, compared with the outcome achieved in patients treated by the Oslo cleft team.

In *Chapter 6*, dental arch relationship was assessed in an international setting with the recently developed EUROCRAN Index. The outcome in the Warsaw group was compared with the results achieved in patients treated by the Nijmegen Cleft Palate Craniofacial Unit.

In *Chapter 7*, nasolabial esthetics was assessed in an international setting and compared with nasolabial appearance of patients treated by the Nijmegen Cleft Palate Craniofacial Unit.

In *Chapter 8*, the most noteworthy findings are discussed. Some suggestions for future research are given.

1.8 References

1. Mossey PA, Little J, Munger RG, Dixon MJ, Shaw WC. Cleft lip and palate. *Lancet* 2009;374:1773-85.
2. Hayes C. Environmental risk factors and oral clefts. In Cleft lip and palate. From origin to treatment. Ed. Wyszynski DF, Oxford University Press, New York 2002;159-69.

3. Chung KC, Kowalski CP, Kim HM, Buchman SR. Maternal cigarette smoking during and the risk of having a child with cleft lip/palate. *Plast Reconstr Surg* 2000;105:485-91.
4. Shaw GM, Lammer EJ. Maternal periconceptional alcohol consumption and risk for orofacial clefts. *J Pediatr* 1999;134:298-303.
5. Romitti PA, Lidral AC, Munger RG, Daack-Hirsch S, Burns TL, Murray JC. Candidate genes for nonsyndromic cleft lip and palate and maternal cigarette smoking and alcohol consumption: evaluation of genotype-environment interactions from a population-based case-control study of orofacial clefts. *Teratology* 1999;59:39-50.
6. Romitti PA, Sun L, Honein MA, Reefhuis J, Correa A, Rasmussen SA. Maternal periconceptional alcohol consumption and risk of orofacial clefts. *Am J Epidemiol* 2007;166:775-85.
7. Hecht JT, Annegers JF. Familial aggregation of epilepsy and clefting disorders: a review of the literature. *Epilepsia* 1990;31:574-7.
8. Hecht JT, Annegers JF, Kurland LT. Epilepsy and clefting disorders: lack of evidence of a familial association. *Am J Med Genet* 1989;33:244-7.
9. Czeizel AE, Rockenbauer M. Population-based case-control study of teratogenic potential of corticosteroids. *Teratology* 1997;56:335-40.
10. Shaw GM, Lammer EJ, Wasserman CR, O'Malley CD, Tolarova MM. Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally. *Lancet* 1995;346:393-6.
11. Wong WY, Eskes TK, Kuijpers-Jagtman AM, Spauwen PH, Steegers EA, Thomas CM, Hamel BC, Blom HJ, Steegers-Theunissen RP. Nonsyndromic orofacial clefts: association with maternal hyperhomocysteinemia. *Teratology* 1999;60:253-7.
12. Oberoi S, Vargervik K. Hypoplasia and hypodontia in Van der Woude syndrome. *Cleft Palate Craniofac J* 2005;42:459-66.
13. Mossey P. Epidemiology underpinning research in the aetiology of orofacial clefts. *Orthod Craniofac Res* 2007;10:114-20.
14. Christensen K. The 20th century Danish facial cleft population - epidemiological and genetic-epidemiological studies. *Cleft Palate Craniofac J* 1999;36:96-104.
15. Kernahan DA, Stark RB. A new classification for cleft lip and cleft palate. *Plast Reconstr Surg Transplant Bull* 1958;22:435-41.

16. Mossey PA, Little J. Epidemiology of oral clefts: an international perspective. In Cleft Lip and Palate. From Origin to Treatment. Ed. Wyszynski DF, Oxford University Press, New York 2002;127-58.
17. Croen LA, Shaw GM, Wasserman CR, Tolarová MM. Racial and ethnic variations in the prevalence of orofacial clefts in California, 1983-1992. *Am J Med Genet* 1998;79:42-7.
18. Vanderas AP. Incidence of cleft lip, cleft palate, and cleft lip and palate among races: a review. *Cleft Palate J* 1987;24:216-25.
19. Antoszewski B, Kruk-Jeromin J: Częstość występowania rozszczepów wargi i(albo) podniebienia u dzieci łódzkich w latach 1982-1991. *Pol Merkur Lekarski* 1997;3:10-2.
20. Antoszewski B, Kruk-Jeromin J. Epidemiology of cleft lip and palate in Lodz, Poland, in the years 1981-1995. *Acta Chir Plast* 1997;39:109-12.
21. Antoszewski B, Kruk-Jeromin J: Analiza częstości występowania rozszczepów wargi i/lub podniebienia oraz typów wady na terenie województwa łódzkiego w latach 1996-2000. *Ortopedia Szczękowa Ortodoncja* 2002;2:3-6.
22. Małkiewicz EH, Kaczmarek E: Epidemiologia rozszczepów podniebienia pierwotnego i/lub wtórnego w wybranych regionach Polski w latach 1998-1999. *Czas Stomat* 2005;58:917-24.
23. Fogh-Andersen P. Inheritance of Harelip and Cleft Palate. Munksgaard, Copenhagen 1942.
24. Wyszynski DF, Beaty TH, Maestri NE. Genetics of nonsyndromic oral clefts revisited. *Cleft Palate Craniofac J* 1996;33:406-17.
25. Jensen BL, Kreiborg S, Dahl E, Fogh-Andersen P. Cleft lip and palate in Denmark, 1976–1981: epidemiology, variability, and early somatic development. *Cleft Palate J* 1988;25:258–69.
26. Hagberg C, Larson O, Milerad J. Incidence of cleft lip and palate and risks of additional malformations. *Cleft Palate Craniofac J* 1998;35:40-5.
27. Tolarová M. Orofacial clefts in Czechoslovakia. Incidence, genetics and prevention of cleft lip and palate over a 19-year period. *Scand J Plast Reconstr Surg Hand Surg* 1987;21:19–25.
28. Semb G, Shaw WC. Facial growth in orofacial clefting disorders. In: Turvey TA, Vig KWL, Fonseca RJ eds. Facial Clefts and Craniosynostosis. Principles and Management. Philadelphia: WB Saunders; 1996:28-56.
29. Semb G. A study of facial growth in patients with unilateral cleft lip and palate treated by the Oslo CLP Team. *Cleft Palate Craniofac J* 1991;28:1-21.

30. Kremenak CR, Huffman WC, Olin WH. Growth of maxillae in dogs after palatal surgery. Part I. *Cleft Palate J* 1967;4:6-17.
31. Kremenak CR, Huffman WC, Olin WH. Growth of maxillae in dogs after palatal surgery. Part II. *Cleft Palate J* 1970;7:719-36.
32. Leenstra TS, Kuijpers-Jagtman AM, Maltha JC, Freihofer HP. Palatal surgery without denudation of bone favours dentoalveolar development in dogs. *Int J Oral Maxillofac Surg* 1995;24:440-4.
33. Ishikawa H, Nakamura S, Misaki K, Kudoh M, Fukuda H, Yoshida S. Scar tissue distribution on palates and its relation to maxillary dental arch form. *Cleft Palate Craniofac J* 1998;35:313-9.
34. Kim T, Ishikawa H, Chu S, Handa A, Iida J, Yoshida S. Constriction of the maxillary dental arch by mucoperiosteal denudation of the palate. *Cleft Palate Craniofac J* 2002;39:425-31.
35. Fujioka M, Fujii T. Maxillary growth following atelocollagen implantation on mucoperiosteal denudation of the palatal process in young rabbits: implications for clinical cleft palate repair. *Cleft Palate Craniofac J* 1997;34:297-308.
36. Meng T, Shi B, Lu DW, Li Y, Wu M. Roles of palatine bone denudation repairing with free buccal or palatal mucosal graft on maxillary growth: an experimental study in rabbits. *Ann Plast Surg* 2007;59:323-8.
37. Shaw WC, Semb G, Nelson P, Brattström V, Mølsted K, Prahl-Andersen B. The Eurocleft Project 1996-2000. Standards of care for cleft lip and palate in Europe. Amsterdam: IOS Press, 2000.
38. Gillies HG, Fry WK. A new principle in the surgical treatment of congenital cleft palate and its mechanical counterpart. *Br Med J* 1921;1:335-9.
39. Schweckendieck H. Zur Frage der Früh- und Spät-operation der angeborenen Lippen-Kiefer-Gaumen-spalten. *Z Laryng* 1951;30:51-6.
40. Ross RB. Treatment variables affecting facial growth in complete unilateral cleft lip and palate. *Cleft Palate J* 1987;24:5-77.
41. Hotz M, Gnoinski W. Comprehensive care of cleft lip and palate children at Zürich university: a preliminary report. *Am J Orthod.* 1976;70:481-504.
42. Hotz M. 22 years of experience in cleft palate management, and its consequences for treatment planning. In: Kehrer B, Slongo T, Graf B, Bettex M, eds. Long Term Treatment in Cleft Lip and Palate. Bern: Hans Huber; 1981:208–11.

43. Robertson NRE, Jolleys A. A further look at the effects of delaying repair of the hard palate. In: Huddart AG, Ferguson MJW, eds. Cleft Lip and Palate. Vol. 2. Long-term Results and Future Prospects. Manchester: University Press; 1990:176–82.
44. Chait L, Gavron G, Graham C, Noik E, De Aguiar G. Modifying the two-stage cleft palate surgical correction. *Cleft Palate Craniofac J* 2002;39:226–32.
45. Friede H. Maxillary growth controversies after two-stage palatal repair with delayed hard palate closure in unilateral cleft lip and palate patients: perspectives from literature and personal experience. *Cleft Palate Craniofac J* 2007;44:129-36.
46. Cosman B, Falk AS. Delayed hard palate repair and speech deficiencies: a cautionary report. *Cleft Palate J* 1980;17:27-33.
47. Bardach J, Morris HL, Olin WH. Late results of primary veloplasty: the Marburg Project. *Plast Reconstr Surg* 1984;73:207-18.
48. Rohrich RJ, Rowsell AR, Johns DF, Drury MA, Grieg G, Watson DJ, Godfrey AM, Poole MD. Timing of hard palatal closure: a critical long-term analysis. *Plast Reconstr Surg* 1996;98:236-46.
49. Holland S, Gabbay JS, Heller JB, O'Hara C, Hurwitz D, Ford MD, Sauder AS, Bradley JP. Delayed closure of the hard palate leads to speech problems and deleterious maxillary growth. *Plast Reconstr Surg* 2007;119:1302-1310.
50. Farina R. Total unilateral harelip: correction of severe deformity of the palate and lips in a single operation; Le Mesurier's cheiloplasty & Veau-Ernst's gnatho-urano-staphyloplasty. In French. *Ann Chir Plast* 1958;3:199-205.
51. Davies D. The one-stage repair of unilateral cleft lip and palate: a preliminary report. *Plast Reconstr Surg* 1966;38:129-36.
52. Kaplan I, Dresner J, Gorodischer C, Radin L. The simultaneous repair of cleft lip and palate in early infancy. *Br J Plast Surg* 1974;27:134-8.
53. Kaplan I, Taube E, Ben-Bassat M, Dresner J, Nachmani A, Rosenbaum M. Further experience in the early simultaneous repair of cleft lip and palate. *Br J Plast Surg* 1980;33:299-300.
54. Kaplan I, Ben-Bassat M, Taube E, Dresner J, Nachmani A. Ten-year follow-up of simultaneous repair of cleft lip and palate in infancy. *Ann Plast Surg* 1982;8:227-8.
55. Hönigmann K. One-stage closure of uni-and bilateral cleft lip and palate. *Brit J Oral Maxillofac Surg* 1996;34:214-9.

56. Corbo M, Dujardin T, de Maertelaer V, Malevez C, Glineur R. Dentocraniofacial morphology of 21 patients with unilateral cleft lip and palate: a cephalometric study. *Cleft Palate Craniofac J* 2005;42:618-24.
57. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.
58. De Mey A, Swennen G, Malevez C, George M, Mansbach AL. Long-term follow-up of UCLP at the Reine Fabiola Children's Hospital. *B-ENT* 2006;2:44-50.
59. Fudalej P, Obłoj B, Dudkiewicz Z Budowa i położenie żuchwy u osób z całkowitym jednostronnym rozszczepem wargi i podniebienia leczonych metodą jednoetapową. *Med Wieku Rozwoj* 2006; X(3) część II:875-84.
60. Fudalej P, Obłoj B, Dudkiewicz Z Budowa twarzoczaszki 10-latków z jednostronnym całkowitym rozszczepem wargi i podniebienia leczonych metodą jednoczasową. *Med Wieku Rozwoj* 2007;XI (1):45-50.
61. Dudkiewicz Z. Jednoetapowe leczenie rozszczepu podniebienia pierwotnego i wtórnego. *Pol Przegl Chir* 1985;57:695-9.
62. Dudkiewicz Z. Ocena jednoetapowego chirurgicznego leczenia jednostronnych rozszczepów podniebienia pierwotnego i wtórnego. *Probl Chir Dziec* 1991;18:8-19.
63. Dudkiewicz Z. Wielokierunkowa ocena zastosowanej własnej jednoetapowej metody w leczeniu chirurgicznym jednostronnych całkowitych rozszczepów podniebienia pierwotnego i wtórnego. Praca habilitacyjna z kliniki Chirurgii Dzieci i Młodzieży, Warszawa 1990.
64. Kulewicz M. Cefalometryczna ocena późnych wyników leczenia jednostronnych całkowitych rozszczepów wargi i podniebienia. Praca doktorska z Kliniki Chirurgii Dzieci i Młodzieży, Warszawa 2002.
65. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercenter study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93-8.
66. Roberts CT, Semb G, Shaw WC. Strategies for the advancement of surgical methods in cleft lip and palate. *Cleft Palate Craniofac J* 1991;28:141-9.
67. Feinstein AR. Epidemiologic analyses of causation: The unlearned scientific lessons of randomized trials. *J Clin Epidemiol* 1989;42:481-9.

Chapter 2

Midfacial growth in a consecutive series of preadolescent children with complete unilateral cleft lip and palate following a one-stage simultaneous repair

Piotr Fudalej
Barbara Obloj
Dorota Miller-Drabikowska
Anna Samarcew-Krawczak
Zofia Dudkiewicz

Cleft Palate Craniofac J 2008;45:667-73

Summary

Objective: To evaluate midfacial growth in prepubertal children with complete unilateral cleft lip and palate following one-stage simultaneous repair.

Subjects: A series of 28 consecutively treated subjects with complete unilateral cleft lip and palate were compared with age- and gender-matched controls with normal midfacial structure.

Methods: On the lateral cephalograms taken at the age of approximately 10 years, size and position of the maxilla and upper dental arch were evaluated in vertical and horizontal planes. Statistical analysis included independent t tests and nonparametric Mann-Whitney tests.

Results: The maxilla was found to be retruded (sella-nasion-point A angle decreased by 4.5^0 and nasion to point A distance increased by 4.2 mm) and rotated posteriorly (sella-nasion/palatal plane angle decreased by 4.5^0) in the cleft group. Maxillary length (pterygomaxillare-point A distance) was diminished by approximately 2 mm. Upper incisors were found retroclined in comparison to controls (both upper incisor axis/sella-nasion and upper incisor axis/palatal plane angles were decreased by 10.7^0 and 6.1^0, respectively).

Conclusions: Maxillary prominence, as measured with the sella-nasion-point A angle and the condylion-point A and articulare-point A distances, was decreased. Shortened length and posterior position of the maxillary body were responsible at a ratio of 60% to 40% for a decreased prominence of the maxillary complex. The palatal plane demonstrated a larger inclination to the sella-nasion plane by 4.5^0 due to a decreased sella-posterior nasal spine distance.

2.1 Introduction

One-stage simultaneous repair of the complete unilateral cleft lip and palate is infrequently performed in the cleft centers worldwide despite more than 40 years since its introduction.[1] The concept of one-stage approach assumed that during one surgical session all the cleft structures were repaired to promote relatively undisturbed craniofacial growth, but there is little evidence to support this hypothesis. Several studies published so far offer personal opinion as to details of the surgical technique.[2-5] Long-term follow-up, especially regarding facial growth, of children with complete unilateral cleft lip and palate subjected to one-stage repair is very limited.[6,7] Corbo et al.[6] compared a sample of children with unilateral cleft lip and palate who underwent two surgical protocols (11 subjects had simultaneous repair at the 3rd month of life; 10 subjects had the soft palate repaired at 3 months and lip and hard palate repaired at 6 months) with normal controls and found maxillary retrusion and a steeper palatal plane in the cleft groups. No difference between the two protocols was observed. Savaci et al.[7] followed two groups of children with cleft subjected to one-stage repair (19 subjects) or two-stage closure (22 subjects). They found that at 7 years, the maxillomandibular complex was retrognathic in both cleft groups relative to noncleft controls, the palatal plane was more open, anterior facial height was larger, and posterior facial height decreased. They did not detect any difference between the two cleft groups. However, these studies suffer from serious shortcomings such as a selection of non-consecutive cases to the sample (Savaci et al.[7] reported drop-out rate of about 31%) or small sample size.6 Moreover, Corbo and colleagues' suggestion as to retrognathic position of the maxillomandibular complex in children with cleft is inconsistent with values of some cephalometric measurements reported in the study. Therefore, in order to draw firm conclusions regarding facial growth following one-stage repair, a larger sample of consecutive patients should be examined.

The purpose of this study is to evaluate morphology of the maxillary complex in a consecutive series of preadolescent children with complete unilateral cleft lip and palate following one-stage simultaneous repair.

2.2 Subjects

2.2.1 Sample

Files of the Centre for Craniofacial Disorders, Institute of Mother and Child (IMC), Warsaw, Poland were searched for individuals diagnosed with complete unilateral cleft lip and palate who had been treated consecutively with one-stage simultaneous repair. All subjects had to have good quality lateral cephalograms taken at the age of approximately 10 years. Additional selection criteria included Polish ethnicity and absence of any associated syndrome. This study was approved by the Bioethics Committee of the IMC.

2.2.2 Surgical management

One-stage simultaneous closure of the complete unilateral cleft lip and palate has been carried out for more than 20 years at the IMC. This method has undergone several modifications since the first time it was performed, and the most recent one was introduced in May 1993. During the one-stage operation, the lip and hard and soft palates are repaired according to the following protocol: lip repair is undertaken by a triangular flap; for hard palate repair an extended vomer flap with a tight closure of the anterior palate is performed; soft palate repair is performed by dissection of all abnormal muscle insertions from the posterior margin of the hard palate up to the pterygoid hamuli, which are always fractured. No presurgical orthodontic treatment is carried out.

2.2.3 Controls

Age and sex-matched individuals of Polish ethnicity who met the following inclusion criteria were chosen for the control group: Angle Class I, no crossbite, positive overbite <5 mm, mild crowding (Incisor Irregularity Index <3.5 mm), and harmonious facial build.

2.3 Methods

Cephalograms were scanned with a PowerLook III (UMAX) scanner (Taipei, Taiwan). Cephalometric analysis was carried out with NemoCeph NX 2005 program (Nemotec, Madrid, Spain). Because cephalograms demonstrated different magnification, adjustment for enlargement factor was made. The identified landmarks and angular and linear measurements are presented in Table 1 and Figures 1 and 2.

2.3.1 Error of method:

The measurement errors were calculated from the equation:

$$S_X = \sqrt{\frac{\Sigma D^2}{2N}}$$

with D representing the difference between corresponding first and second measurements on 20 (N) randomly selected cephalograms (10 cleft and 10 normal subjects) made at least 1 week apart.

Table 1 Description of the cephalometric measurements.

Variable code	Symbol	Description
1.	S-N	sella – nasion distance
2.	S-Ba	sella – basion distance
3.	NSBa	nasion – sella – basion angle
4.	Co-A	condylion to point A distance
5.	Ar-A	articulare to point A distance
6.	Ptm-A	pterygomaxillare to point A distance
7.	Ar-N H	articulare to nasion through horizontal plane distance
8.	Ar-Ptm H	articulare to pterygomaxillare through horizontal plane distance
9.	Ptm-A H	pterygomaxillare to point A through horizontal plane distance
10.	A-N H	point A to nasion through horizontal plane distance
11.	N-ANS	nasion to anterior nasal spine distance
12.	S-PNS	sella to posterior nasal spine distance
13.	N-ANS V	nasion to anterior nasal spine through vertical plane distance
14.	S-PNS V	sella to posterior nasal spine through vertical plane distance
15.	SNA	sella – nasion – point A angle
16.	SN/PP	sella – nasion / palatal plane angle
17.	SN/OP	sella – nasion / occlusal plane angle
18.	PP/OP	palatal plane / occlusal plane angle
19.	U1/SN	upper incisor axis / sella – nasion angle
20.	U1/PP	upper incisor axis / palatal plane angle
21.	U1e-PP	upper incisor edge (U1e) to palatal plane distance
22.	U1e-NA	upper incisor edge (U1e) to nasion – point A line distance
23.	U6c-PP	mesial cusp of the first molar (U6c) to palatal plane distance
24.	U1e-U6c	upper incisor edge to mesial cusp of the first molar distance

2.3.2 Statistical analysis

Means and standard deviations were calculated for each measurement. Shapiro-Wilk tests were carried out to evaluate normality of distribution in each group, and Levene tests were computed to assess differences in variance of each measurement.

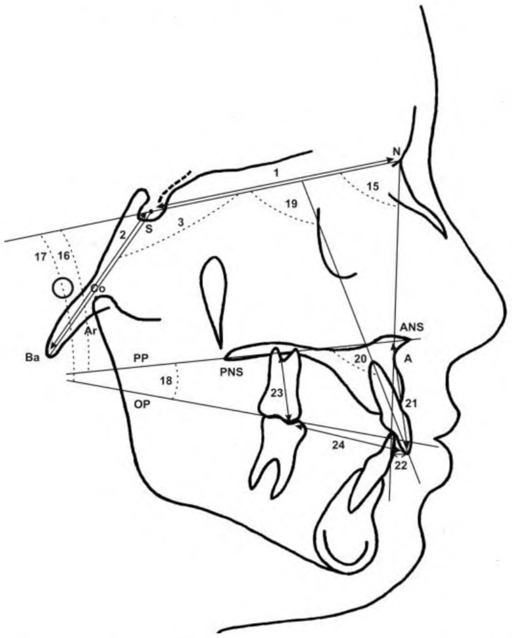


Figure 1 Angular and direct linear cephalometric measurements. Numbers correspond to variable codes from Table 1

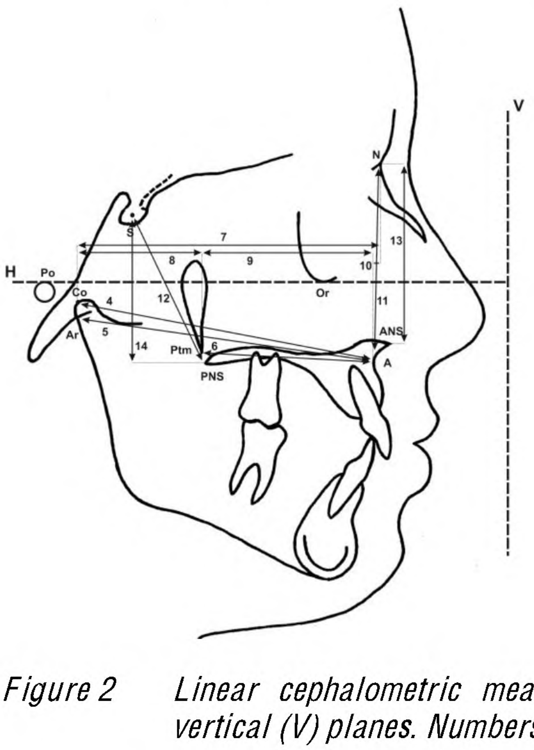


Figure 2 Linear cephalometric measurements in relation to horizontal (H) and vertical (V) planes. Numbers correspond to variable codes from Table 1

In the case of normal distribution and equal variance in both groups, independent t-tests were carried out to test the intergroup difference in measurements. Otherwise, nonparametric Mann-Whitney rank sum tests were performed. The difference was considered significant for $p < .05$. The 95% confidence intervals (CI) were calculated for the difference of means for each variable.

2.4 Results

2.4.1 Sample

Among 225 patients who had repair of the different forms of cleft at the IMC from December 1, 1994, through July 31, 1996, there were 29 patients with complete unilateral cleft lip and palate who were treated with one-stage simultaneous repair. Twenty-eight subjects were finally selected (1 subject was excluded for an associated mental retardation). All of them were operated on by the same experienced surgeon (Z.D.). Two out of 28 subjects have never received any other treatment, except for the cleft repair in the first year of life.

Characteristics of the groups are presented in Table 2. The distribution of gender was balanced, with approximately 70% of both groups comprising boys. Although mean age of the cleft group was 0.3 years older than that of the control group, no statistically significant difference was detected ($p = .117$). Mean age when the one-stage repair was performed was 8.8 months (SD = 1.4), somewhat later in boys (9.1 months; SD = 1.4; range 7 to 13 months) than in girls (8.1 months; SD = 1.2; range 6 to 10 months).

Table 2 Distribution of gender and age (in years) in the cleft and normal groups.

	Cleft group					Normal group				
	N	%	Mean	SD	Range	N	%	Mean	SD	Range
Males	20	71.4	10.60	0.92	8.1 - 12.2	22	68.8	10.27	0.58	9.2 - 11.1
Females	8	28.6	10.73	0.83	10.0 - 12.3	10	31.2	10.47	0.52	9.7 - 11.2
	28		10.63	0.88		32		10.33	0.56	

2.4.2 Error of measurements

The error of measurements did not exceed 1.5 mm or 1.5^0, a value observed by other investigators.[8,9]

Table 3 *Intergroup differences in measured variables detected by independent t tests or Mann-Whitney rank sum tests (†); 95% Confidence Interval (CI) calculated for the difference between means.*

Variable	Cleft group		Normal group		Difference	95% CI	
	Mean	*SD*	*Mean*	*SD*		*Lower limit*	*Upper limit*
S-N†	63.38	2.96	63.52	2.45	-0.14	-1.28	1.56
S-Ba	39.12	3.30	39.45	2.70	-0.33	-1.22	1.88
NSBa	132.49	4.68	131.09	5.24	1.41	-3.99	1.18
Co-A	75.83	3.92	78.49	2.92	-2.67**	0.90	4.44
Ar-A	73.37	3.70	76.53	3.50	-3.16**	1.29	5.02
Ar-N H	78.40	5.12	77.59	4.35	0.81	-3.26	1.64
Ar-Ptm H	29.62	2.48	30.99	2.44	-1.37**	0.10	2.65
Ptm-A H	41.45	3.08	43.48	2.48	-2.04*	0.60	3.48
Ptm-A	43.86	3.08	45.56	2.50	-1.70*	0.26	3.15
SNA	75.53	4.06	79.98	3.35	-4.45***	2.54	6.36
A-N H	7.34	5.19	3.13	3.63	4.21***	1.92	6.51
N-ANS†	45.53	3.77	47.10	3.48	-1.57	-0.31	3.46
N-ANS V	45.11	3.75	46.99	3.47	-1.88*	0.01	3.75
S-PNS†	36.56	3.69	41.93	1.86	-5.36***	3.80	6.92
S-PNS V†	33.11	3.79	38.22	2.40	-5.11***	3.44	6.79
SN/PP†	12.90	4.04	8.42	3.52	4.49***	-6.46	-2.51
SN/OP†	22.63	3.53	18.76	4.08	3.88***	-5.84	-1.91
PP/OP	9.73	3.91	10.34	3.14	-0.62	-1.21	2.44
U1/SN	92.25	7.67	102.91	5.50	-10.66***	7.24	14.08
U1/PP†	105.17	7.80	111.31	5.18	-6.14**	2.65	9.64
U1ePP	24.50	3.03	24.54	2.39	-0.04	-1.36	1.45
U1eNA†	1.69	2.32	3.60	1.46	-1.91***	0.89	2.94
U6cPP	20.83	2.11	18.79	2.51	-2.04***	-3.25	-0.84
U1e-U6c†	25.48	3.53	30.52	2.08	-5.04***	-6.57	-3.50

$^* p < 0.05$. $^{**} p < 0.01$. $^{***} p < 0.001$

2.4.3 Cranial base

No inter-group differences (Table 3) were detected regarding length of the anterior (S-N; $p = .662$) and middle cranial fossa (S-Ba; $p = .493$) and the cranial flexure angle (NSBa; $p = .257$).

2.4.4 Maxillary spatial position

Position of the maxilla differed significantly between groups, as demonstrated by statistical tests. The maxilla was found retruded in the cleft group versus normal individuals (Figure 3). In the cleft subjects, the more posterior position of point A resulted in a decrease of the SNA angle ($p < .001$) and an increase of the distance from point A to nasion through horizontal plane ($p < .001$).

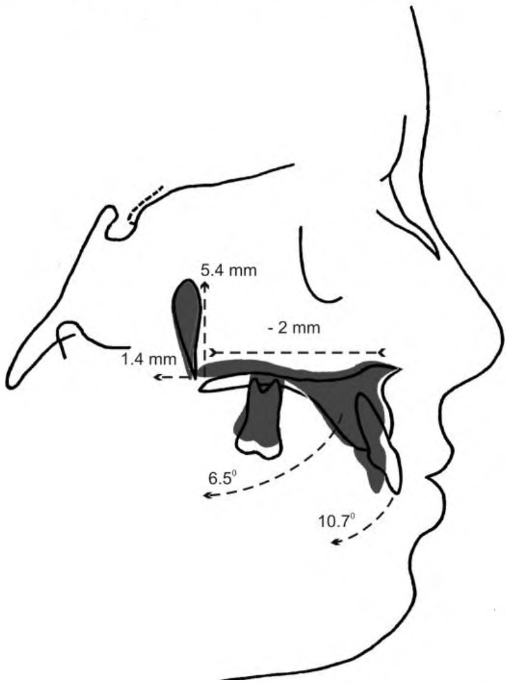


Figure 3 Schematic representation of midfacial morphology in children with cleft (grey) in comparison to controls

Anterior nasal spine (ANS) to nasion distance was decreased by less than 2 mm in the cleft group. The decrease was not statistically significant ($p = .114$) when measurement was performed directly from ANS to nasion landmarks. When the same distance was measured through the vertical plane, statistical significance was detected ($p = .048$). Posterior nasal spine (PNS) to sella distance was diminished by more than 5 mm in individuals with cleft ($p < .001$ for both S-PNS and S-PNS V measurements). As the result of differential changes of N-ANS V and S-PNS V distances, the maxillary body showed a posterior rotation, and the palatal plane / sella-nasion angle increased by almost 4.5^0 ($p < .001$).

2.4.5 Maxillary morphology

Articulare to nasion through one horizontal plane (Ar-N H) distance, in relation to which the maxillary size and position had been determined, was similar in both groups (p = .509). Comparison of particular compartments, namely a distance from articulare to the posterior border of the maxillary body, the body of the maxilla, and anterior border of the maxillary body to nasion (Ar-Ptm H, Ptm-A H, and A-N H, respectively) reveals intergroup differences. The maxillary body (Ptm-A H) in the individuals with cleft is shorter by 2 mm than in subjects without cleft (p = .006). The space distal to the maxillary body (Ar-Ptm H) is less in the cleft group by about 1.4 mm (p = .035), and the position of the anterior border of the maxillary body is retruded, as demonstrated by an increase of A-N H distance by about 4.2 mm (p = .001) in the cleft group versus the control group.

Maxillary length, measured from both condylion and articulare landmarks to point A (Co-A and Ar-A, respectively), was also approximately 3 mm less in the subjects with cleft than in controls (p = .004 and .001, respectively).

2.4.6 Dental arch

The upper incisors were found retroclined in the cleft group in comparison to the control group. Both the angle between the axis of the central incisors and sella-nasion line (U1/SN) and the axis of the central incisors and palatal plane (U1/PP) was decreased, by 10.7^0 and 6.1^0, respectively (p < .001 and .001, respectively). Retroclination of the upper central incisors translated into increased distance from incisal edge to the nasion-point A line (U1-NA) by 1.9 mm in the cleft group as compared with the control group (p < .001). The length of the dental arch in the individuals with cleft was less than that in controls: distance from the edge of the central incisor to the mesial cusp of the first molar (U1e-U6c) was shortened by approximately 5 mm (p < .001). Occlusal to palatal plane inclination (PP/OP) was similar in both groups (p = .502).

2.5 Discussion

Since January 2000, the *Cleft Palate-Craniofacial Journal* has included 41 studies describing midfacial growth in individuals with cleft following different treatment protocols. In only nine of them did the authors draw conclusions based on a sample of consecutively treated patients, despite the fact that when selected cases, as opposed to consecutive ones, are studied, a risk of selection bias occurs. Consequently, formulated conclusions may not be entirely valid. On the other hand, the collection of consecutive cases is often impossible due to reasons unrelated to the work of a cleft team. Expenses associated with transportation and accommodation in Poland certainly reduce attendance in the orthodontic clinic at the IMC once the surgical repair is complete. The example of two children from our sample who were examined by one investigator (P.F.) at their hometowns located more than a hundred miles from Warsaw demonstrates what extra efforts were necessary to gather records of a series of consecutively treated patients in order to strengthen the validity of our conclusions.

Although growth disturbances in children with complete unilateral cleft lip and palate are not restricted to the maxilla,[10,11] the scope of this study was purposefully limited to maxillary complex for two reasons: the maxillary complex is most severely affected by the cleft itself, and there are no detailed data regarding the structure and spatial position of the maxilla following one-stage repair.

The findings of this study show that maxillary prominence is less in the cleft group than in the control group. Both the SNA angle and linear measurements frequently used to evaluate anteroposterior position of the maxilla, such as condylion-point A and articulare-point A, are diminished following a one-stage approach. This is in agreement with other studies that evaluated maxillofacial morphology in preadolescent children. Brattström et al.,[12] in a summary of a part of the Eurocleft project that dealt with craniofacial form of 9- and 12-year-old children subjected to various treatment protocols in five Northern European cleft centers, found similar values of the SNA angle. Although the design of Eurocleft project was intercenter comparison without noncleft controls, when published cephalometric norms are consulted,[13-15] it is clear that children with cleft demonstrated a decreased SNA angle by several degrees no matter in which cleft center they were treated. Semb[10] studied a longitudinal sample of 257 subjects with complete unilateral cleft lip and palate and found maxillary prominence in 10-year-olds similar to that found in Polish peers. Öztürk and Cura[16] compared 20 children of Turkish ethnicity with unilateral cleft lip and palate with 20 noncleft subjects matched according to age and sex, and they found the SNA angle reduced by about 4.5^{0}, a value found in this study. Savaci et al.[7] examined a sample of 41 individuals with cleft that had undergone either a one-stage (19 children) or two-stage (22 children) repair and compared them with noncleft controls. They concluded that maxillary prominence is reduced in children with cleft and the SNA is decreased by approximately 4.5^{0}. Contrary conclusions were arrived at by Trotman et al.,[17] who performed an intercenter comparison of 43 bone-grafted versus 43 nongrafted children with cleft and found that the SNA angle in nongrafted subjects approximated the norm. However, the wide age range (from 5 to 16) and the nonconsecutive cases in the samples lessen the strength of this finding. Also, the findings of Corbo et al.,[6] who evaluated facial morphology following one- and two-stage surgical protocols, disagree with the results of this study. Corbo et al. found maxillary prominence, especially in one-stage group, similar to the norm. A possible explanation for disagreement between the results of Corbo et al. and ours is small sample size (10 subjects in a one-stage group) and the use of selected rather than consecutively treated patients.

Two factors, namely (1) shortened length and (2) posterior position of the maxillary body, are responsible at a ratio of 60% to 40% for a decreased prominence of the maxillary complex found in our cleft group. The decreased length of the maxillary body found in our sample was indirectly confirmed by Mølsted et al.,[18] who examined craniofacial form in 9-year-olds with cleft from five European cleft centers. They found that pterygomaxillare (Ptm) to point A distance did not demonstrate intercenter difference and was similar to the value found in our investigation. Smahel and Mullerova[19] examined three groups of individuals with unilateral cleft lip and palate that had undergone various surgical protocols and concluded that there was no intergroup difference for maxillary length. Johnston et al.[20] investigated long-term growth following two surgical protocols in a sample of 34 children, all 10 years of age, and observed a maxillary length identical to that in our subjects. Also, Semb[10] reported maxillary length in 10-year-olds following the Oslo treatment protocol to be just 0.7 mm longer than that in the Polish sample. No study was identified that provided data regarding a change of the compartment posterior to the maxillary body. One should keep in mind that in order to draw firm conclusions regarding maxillary size in preadolescent children that underwent surgical (and orthodontic) treatment, a noncleft control derived from the same population is indispensible. The above-cited studies were inter- or intercenter comparisons that aimed to investigate which protocol resulted in better growth, and no control group comprising children without cleft was included. Consequently, even if the maxillary size was the same in the various samples, potential differences among underlying populations prevent us from concluding that all protocols have the same impact on the morphology of the maxilla.

The surgical protocol developed at the IMC aims to leave maxillary bone surface without denudation to eliminate granulation and subsequent scar formation. One of the prerequisites to achieve this goal is a dissection of all muscle insertions from the posterior margin of the hard palate up to the pterygoid hamuli. An area posterior to the hard palate is assumed to have the most scar tissue of all regions that restricts further growth. A steeper palatal plane and reduction of S-PNS distance suggest this assumption may hold true. Comparison with other studies yields unequivocal conclusions. Although in most of the investigated samples the S-PNS measurement is larger than that in our subjects[10,12,21] differences are relatively small, within a range of 2 mm. Inclination of the palatal plane to cranial base (SN/PP) in our sample is the steepest of all found in the studies that described facial morphology in preadolescent children,[6,7,10,12,16,19-22] however, in the one investigation that used noncleft controls,[6] an increase of palatal plane inclination exceeded the alteration detected in our study by more than.[20]

In this study, the cranial base angle (NSBa), length of anterior cranial fossa (S-N), and length of clivus (S-Ba) did not show intergroup difference. Previous investigations produced conflicting results. Mars and Houston[23] and Capelozza et al.[24] noted no difference in the cranial base angle. Bishara et al.[25] observed reduced cranial base angle, whereas Shetye and Evans[26] observed enlarged cranial base angle in unoperated cleft patients. In a surgically repaired cleft lip and palate sample, as opposed to Ross[27] and Dahl[28] who noticed a larger cranial base angle, Harris[29] observed a reduced cranial base angle. Sandham and Cheng[30] also found a reduced cranial base angle but only in girls. A similar erratic pattern of findings was noted also for S-N and S-Ba measurements. A possible explanation for disagreement between the outcomes of various studies is the type of control group used. Most investigations used noncleft controls who might have demonstrated malocclusion associated with reduction or enlargement of cranial base dimensions. In addition, a large age range of subjects in the samples and interpopulation differences might have contributed to the observed contradictory results.

Cephalometric evaluation of our sample of 28 consecutively treated patients with complete unilateral cleft lip and palate demonstrates that midfacial growth in preadolescence after a one-stage repair resembles, in many aspects, growth changes reported in other publications. This investigation also points to fundamental problems that prevent us from making firm conclusions when the results of this study are juxtaposed with other reports. Most studies are inter- or intracenter comparisons of particular protocols or surgical techniques, and the results are not assessed in the context of the population from which the children with cleft originated. Sample size and the requirement of consecutive cases, as opposed to nonconsecutive ones, are interrelated. By increasing the number of subjects in the sample, one can raise power to detect smaller intergroup differences (Table 4). As discussed before, however, accumulation of a large number of consecutive cases is often impossible. A relatively small number of children with cleft in the sample also may increase susceptibility bias,[31] which occurs when cases with inequivalent initial severity of the cleft are grouped together. Only a larger sample size lessens this bias.

Table 4 Relation between sample size and power to detect intergroup difference with t test for independent samples.

Difference planned to detect (mm or ^{0})	Assumed SD	N per group to achieve 80% power	Assumed SD	N per group to achieve 80% power
1	3	143	4	253
2	3	37	4	64
3	3	17	4	29

2.6 Conclusions

Based on the results of this study, the following can be concluded:
(1) Maxillary prominence, as measured with the SNA angle and condylion-point A and articulare-point A distances, is decreased.
(2) Shortened length and posterior position of the maxillary body are responsible at a ratio of 60% to 40% for a decreased prominence of the maxillary complex.
(3) Palatal plane demonstrates larger inclination by 4.5^0 due to a decreased sella-PNS distance.
(4) Upper incisors are retroclined by 6.1^0 in comparison to controls.

2.7 References

1. Davies D. The one-stage repair of unilateral cleft lip and palate: A preliminary report. *Plast Reconstr Surg* 1966;38:129-34.
2. Kaplan I, Dresner J, Gorodischer C, Radin L. The simultaneous repair of cleft lip and palate in early infancy. *Br J Plast Surg* 1974;27:134-8.
3. Lejour M. The effects of simultaneous cleft lip and palate repair on craniofacial growth. *Plast Reconstr Surg* 1989;83:751-2.
4. Alkhairy F. Effect on craniofacial growth of simultaneous cleft lip and palate repair. *Plast Reconstr Surg* 1993;92:379-80.
5. Hönigmann K. One-stage closure of uni- and bilateral cleft lip and palate. *Br J Oral Maxillofac Surg* 1996;34:214-9.
6. Corbo M, Dujardin T, De Maertelaer V, Malevez C, Glineur R. Dentocraniofacial morphology of 21 patients with unilateral cleft lip and palate: a cephalometric study. *Cleft Palate-Craniofac J* 2005;42:618-24.

7. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Sur* 2005;115:1509-17.
8. Mølsted K, Dahl E, Brattstrom V, McWilliam J, Semb G. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: evaluation of maxillary asymmetry. *Cleft Palate Craniofac J* 1993;30:22-8.
9. Swennen G, Berten JL, Kramer FJ, Malevez C, De Mey A, Schwestka-Polly R, Hausamen JE. Mandibular morphology in complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2004;41:403-9.
10. Semb G. A study of facial growth in patients with unilateral cleft lip and palate treated by the Oslo CLP Team. *Cleft Palate Craniofac J* 1991;28:1-21.
11. Fudalej P, Obloj B, Dudkiewicz Z, Hortis-Dzierzbicka M. Mandibular Morphology and Spatial Position Following One-Stage Simultaneous Repair of Complete Unilateral Cleft Lip and Palate. *Cleft Palate Craniofac J* 2008;45:272-7.
12. Brattström V, Mølsted K, Prahl-Andersen B, Semb G, Shaw WC. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 2: craniofacial form and nasolabial appearance. *Cleft Palate Craniofac J* 2005;42:69-77.
13. Bhatia SN, Leighton BC. A Manual of Facial Growth: A Computer Analysis of Longitudinal Cephalometric Growth Data. Oxford University Press, USA 1993;518-43.
14. El-Batouti A, Øgaard B, Bishara SE. Longitudinal cephalometric standards for Norwegians between the ages of 6 and 18 years. *Eur J Orthod* 1994;16:501-9.
15. Thilander B, Persson M, Adolfsson U. Roentgen–cephalometric standards for a Swedish population. A longitudinal study between the ages of 5 and 31 years. *Eur J Orthod* 2005;27:370-89.
16. Öztürk Y, Cura N. Examination of craniofacial morphology in children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1996;33:32-6.
17. Trotman CA, Long RE Jr, Rosenstein SW, Murphy C, Johnston LE Jr. Comparison of facial form in primary alveolar bone-grafted and nongrafted unilateral cleft lip and palate patients: intercentre retrospective study. *Cleft Palate Craniofac J* 1996;33:91-5.

18. Mølsted K, Asher-McDade C, Brattström V, Dahl E, Mars M, McWilliam J, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A Six-Centre International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 2. Craniofacial Form and Soft Tissue Profile. *Cleft Palate Craniofac J* 1992;29:398-404.
19. Šmahel Z, Müllerová Z. Effects of primary periosteoplasty on facial growth in unilateral cleft lip and palate: 10-year follow-up. *Cleft Palate J* 1988;25:356-61.
20. Johnston CD, Leonard AG, Burden DJ, McSherry PF. A comparison of craniofacial form in Northern Irish children with unilateral cleft lip and palate treated with different primary surgical techniques. *Cleft Palate Craniofac J* 2004;41:42-6.
21. Roberts-Harry D, Semb G, Hathorn I, Killingback N. Facial growth in patients with unilateral clefts of the lip and palate: a two-centre study. *Cleft Palate Craniofac J* 1996;33:489-93.
22. Leonard AG, Kneafsey B, McKenna S, Johnston CD, Burden DJ, Stevenson M. A retrospective comparison of craniofacial form in Northern Irish children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1998;35:402-7.
23. Mars M, Houston WJB. A preliminary study of facial growth and morphology in unoperated male unilateral cleft lip and palate subjects over 13 years of age. *Cleft Palate Craniofac J* 1990;27:7–10.
24. Capelozza L, Taniguchi SM, Da Silva OG. Craniofacial morphology of adult unoperated complete unilateral cleft lip and palate patients. *Cleft Palate Craniofac J* 1993;30:376–81.
25. Bishara SE, Krause CJ, Olin WH, Weston D, Ness JV, Felling C. Facial and dental relationships of individuals with unoperated clefts of the lip and/or palate. *Cleft Palate J* 1976;13:238–52.
26. Shetye PR, Evans CA. Midfacial morphology in adult unoperated complete unilateral cleft lip and palate patients. *Angle Orthod* 2006;76:810-6.
27. Ross RB. My friend the cranial base: why it is so normal? *Cleft Palate Craniofac J* 1993;30:511–2.
28. Dahl E. Craniofacial morphology in congenital clefts of the lip and palate. *Acta Odontol Scand* 1970;28(Suppl 57):13–6.
29. Harris EF. Size and form of the cranial base in isolated cleft lip and palate. *Cleft Palate Craniofac J* 1993;30:171–4.
30. Sandham A, Cheng L. Cranial base and cleft lip and palate. *Angle Orthod* 1988; 58:163-8.

31. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93-8.

Chapter 3

Mandibular morphology and spatial position following one-stage simultaneous repair of complete unilateral cleft lip and palate

Piotr Fudalej
Barbara Obloj
Zofia Dudkiewicz
Maria Hortis-Dzierzbicka

Cleft Palate Craniofac J 2008;45:272-7

Summary

Objective: To assess mandibular structure and spatial position following one-stage simultaneous repair of the unilateral cleft lip and palate.

Design: Forty boys and 17 girls with complete unilateral cleft lip and palate who underwent one-stage simultaneous repair of the cleft by the same surgeon at the age of 9.23 months (standard deviation = 1.74) were selected. Lateral cephalograms taken at the age of approximately 10 years were analyzed and were compared with a sex- and age-matched control group that consisted of individuals with Angle Class I, no crossbite, positive overbite < 5 mm, mild crowding (Incisor Irregularity Index < 3.5 mm), and harmonious facial build.

Results: No intergroup differences were demonstrated regarding structure of the cranial base. The mandible was found to be retruded and at a larger inclination to the cranial base as compared with controls. Both total mandibular length (ArGn) and length of the mandibular body were larger in the control group, at < 2 mm. Height of the ramus and gonial angle were similar in both groups. Intergender comparison showed few significant differences in control subjects only (SN, SGo, and NMe variables).

Conclusions: The mandible, following a one-stage simultaneous repair of cleft, was found to be retrusive, and the length of mandibular body was < 2 mm shorter than that of the controls.

3.1 Introduction

Many measures of the treatment outcome in children with complete unilateral cleft lip and palate are based on assessment of the relationship of maxillary and mandibular dental arches. Anterior crossbite,[1] positive overjet,[2] and good dental arch relationship, as measured with the Goslon Yardstick grading system3 all refer to mutual spatial position of upper and lower dental arches, which is directly associated with morphology and position of the maxilla relative to the mandible. Maxillary growth, affected by the cleft and/or its repair, has been researched extensively[4-8] but much less attention has been devoted to alterations of the mandible during growth.

Some animal studies[9-11] suggested that surgical management might impair mandibular development. However, such a relationship between surgical repair of the cleft lip and palate and mandibular growth in humans has not been proven. Comparison of mandibular morphology between Sri Lankan unoperated adults with unilateral cleft lip and palate and normal controls[12] showed that the mandible was smaller and was retruded in individuals with cleft. Capelozza Jr. et al.[13] compared Brasilian adults with different status of the cleft repair (unoperated versus repaired lip versus repaired lip and palate) and concluded that mandibular morphology was similar irrespective of the operation. Da Silva Filho et al.[14] attempted to assess the influence of cleft type on mandibular structure and stated that in all types of cleft examined, the mandible was found retruded relative to normal individuals. When the palate was involved, substantial posterior rotation of the mandible resulted. The implication of Sri Lankan and Brazilian studies was that mandibular retrusion resulted from the cleft itself and was independent of surgical repair. However, a lack of details regarding surgical management[12,15,16] and a wide age range and small sample size[12] presented shortcomings that made it difficult to prove this conclusion. A more recent study[17] assessed mandibular structure following two different surgical protocols, revealed that the type of surgical management might influence mandibular morphology and spatial position. However, intergender differences in response to particular surgical protocols (i.e. gonial angle following the

Hannover protocol was found larger only in boys) and a relatively small sample size made the results of this study difficult to interpret.

A one-stage simultaneous repair of the cleft lip and palate is performed infrequently. The few investigations[18,19] published to date have presented only limited data regarding mandibular structure. Moreover, these studies suffer from limitations such as small sample size and short observation period. Larger, more homogeneous samples and longer observation time might allow more significant conclusions regarding mandibular morphology and position following one-stage simultaneous repair. The purpose of this study was to evaluate mandibular morphology and position following one-stage simultaneous repair of the cleft lip and palate.

3.2 Material and methods

The Bioethics Committee of the Institute of Mother and Child issued an approval for this investigation (reference No 37/2005). Informed consent was obtained from all participants.

3.2.1 Sample

The database of the Centre for Craniofacial Disorders housed at the Institute of Mother and Child (IMC) was searched for subjects of Polish ethnicity who had been diagnosed with complete unilateral cleft lip and palate with no other associated syndrome. Only subjects treated with a one-stage simultaneous repair of the cleft lip and palate by the same experienced surgeon (Z.D.) and having good-quality lateral cephalograms taken at the age of approximately 10 years were selected.

3.2.2 Surgical management

During a one-stage operation the lip and the hard and soft palates were repaired according to the following protocol. Lip repair was undertaken by a triangular flap. For the hard palate repair, an extended vomer flap with a tight closure of the anterior palate was performed. Soft palate repair was performed by dissection of all abnormal muscle insertions from the posterior margin of the hard palate up to the pterygoid hamuli, which were always fractured.

3.2.3 Controls

Age and sex-matched individuals of Polish ethnicity who met the following inclusion criteria were chosen for the control group: Angle Class I, no crossbite, positive overbite < 5 mm, mild crowding (Incisor Irregularity Index < 3.5 mm), and harmonious facial build.

3.2.4 Analysis

Cephalograms were scanned with PowerLook III (UMAX) scanner (Techville, Inc., Dallas, TX). Cephalometric analysis was carried out with NemoCeph NX 2005 program (Nemotec, Madrid, Spain). Because cephalograms demonstrated different magnification, adjustment for enlargement factor was made. The identified landmarks, as well as the angular and linear measurements, are presented in Figure 1.

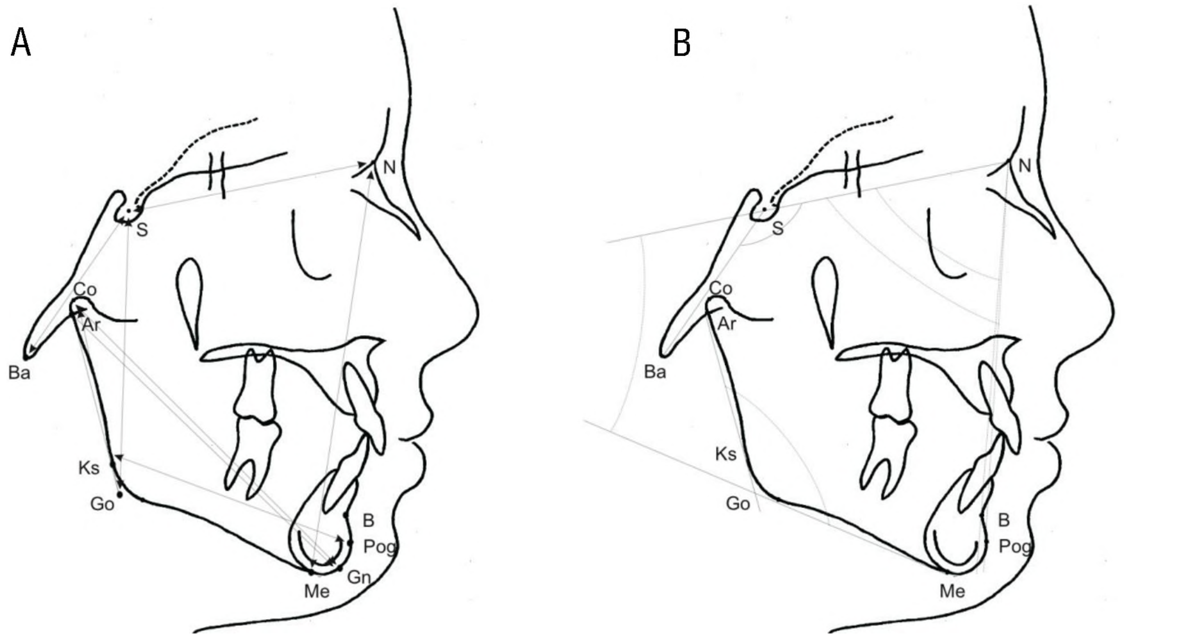


Figure 1 *Landmarks and measurements. A: Linear measurements: SN – anterior cranial fossa length; SBa – medial cranial fossa length; NMe – anterior facial height; SGo – posterior facial height; CoGo and ArGo – mandibular ramus length; CoGn and ArGn – total mandibular length; KsPog and GoMe – mandibular body length. B: Angular measurements: NSBa cranial base flexure; SN/MP – mandibular plane angle; SNB; SNPog; Gonial angle*

3.2.5 *Error of method:*

The measurement errors were calculated from the equation:

$$S_x = \sqrt{\frac{\Sigma D^2}{2N}}$$

with D representing the difference between corresponding first and the second measurements on 20 (N) randomly selected cephalograms (10 cleft and 10 normal subjects) made at least 1 week apart.

3.2.6 *Statistical analysis*

Means and standard deviations were calculated for each measurement. Independent *t* tests were performed to detect intergender difference in variables between cleft (CG) and normal (NG) groups.

Shapiro-Wilk tests were carried out to evaluate normality of the distribution in each group. In case of a normal distribution, independent *t* tests were carried out to test the intergroup difference in measurements. For $p < .05$, the difference was considered significant. For $0.05 \leq p < .1$, the difference was considered marginally significant.

3.3 Results

3.3.1 *Sample*

Characteristics of the groups are presented in Table 1. Gender distribution was balanced, with approximately 70% of both groups comprising boys. The mean age in the CG group was 10.1 years (boys: 10.1 years, range = 8.1 to 12.0; girls: 10.0 years, range = 7.5 to 11.4), whereas the mean age in the NG group was 10.4 years (boys: 10.3 years, range = 9.2 to 11.1; girls: 10.4 years, range = 9.4 to 11.2). The average age at which the one-stage repair was performed was 9.44 months for boys (SD = 1.74; range 6 to 15) and 8.76 months for girls (SD = 1.68; range 6 to 12).

Table 1 Distribution of gender and age (in years) in the cleft (CG) and normal (NG) groups.

Gender	CG			NG		
	N	%	Age (SD)	N	%	Age (SD)
Boys	40	70.2	10.11 (0.85)	38	70.4	10.34 (0.52)
Girls	17	29.8	10.02 (1.01)	16	29.6	10.39 (0.51)
Total	57		10.09 (0.89)	54		10.36 (0.51)

3.3.2 Measurement error

The cephalometric measurement errors are shown in Table 2. For most measurements error did not exceed 1.5 mm or 1.50, a value observed by other investigators.[8,17] Only few variables demonstrated larger error, likely due to difficulty with identification of basion, gonion, and condylion landmarks: NSBa, Gonial angle, and CoGo respectively.

3.3.3 Cranial base

No intergroup differences (Table 3) were detected regarding length of the anterior (SN; p = .622) and middle cranial fossa (SBa; p = .488) and the cranial flexure angle (NSBa; p = .261). Comparison of cranial structure between boys and girls (Table 4) demonstrated slightly longer anterior and middle cranial fossae in boys with normal craniofacial morphology (p = .044 and .091, respectively). No difference between sexes was demonstrated in the CG group.

Table 2 Error of cephalometric measurements.*

Measurement	Cleft group (CG) (n=10)	Normal group (NG) (n=10)
SN (mm)	0.64	0.91
SBa (mm)	1.23	0.79
NSBa (^{0})	1.85	1.92
SNB (^{0})	0.57	0.90
SNPog (^{0})	0.59	1.02
SN/MP (^{0})	0.58	1.25
Gonial angle (^{0})	2.00	1.40
CoGo (mm)	1.51	1.63
ArGo (mm)	1.22	1.17
CoGn (mm)	1.41	1.19
ArGn (mm)	0.94	0.92
KsPog (mm)	0.75	0.71
GoMe (mm)	0.89	0.81
NMe (mm)	0.58	1.29
SGo (mm)	0.52	0.89

**mm – millimeter; ^{0} - degree*

Table 3 Intergroup differences in age and measured variables; p value reflects differences detected by independent t tests.*

Variable	Cleft group	Normal group	*p* value
Age (y)	10.09 (0.89)	10.36 (0.51)	.054
SN (mm)	63.70 (2.98)	63.90 (2.53)	.622
SBa (mm)	38.84 (3.35)	39.26 (3.00)	.488
NSBa (^{0})	131.89 (5.05)	130.80 (5.16)	.261
SNB (^{0})	74.21 (3.64)	77.52 (3.11)	< .001
SNPog (^{0})	75.25 (3.77)	78.33 (3.15)	< .001
SN/MP (^{0})	36.10 (6.07)	32.22 (4.55)	< .001
NMe (mm)	104.85 (5.78)	102.65 (5.92)	.070
SGo (mm)	66.65 (5.48)	67.77 (3.19)	.197
CoGn (mm)	98.79 (6.02)	100.10 (4.67)	.164
ArGn (mm)	92.07 (5.82)	94.00 (4.48)	.047
CoGo (mm)	49.11 (3.87)	49.45 (2.58)	.592
ArGo (mm)	39.50 (3.42)	40.32 (2.78)	.169
KsPog (mm)	69.81 (5.06)	71.44 (3.90)	.050
GoMe (mm)	60.63 (4.91)	62.58 (3.67)	.017
Gonial angle (^{0})	129.41 (7.44)	127.84 (5.10)	.228

**mm – millimeter; ^{0} - degree*

Table 4 Intergender differences in the cleft (CG) and normal (NG) groups assessed with t tests.*

Variable	CG Boys	CG Girls	*p*	NG Boys	NG Girls	*p*
Age (y)	10.11 (0.85)	10.02 (1.01)	.733	10.34 (0.52)	10.39 (0.51)	.769
SN (mm)	64.06 (2.83)	62.86 (3.23)	.169	64.41 (2.36)	62.91 (2.63)	.044
SBa (mm)	39.20 (3.32)	37.99 (3.37)	.219	39.71 (2.95)	38.19 (2.93)	.091
NSBa (^{0})	131.26 (4.85)	133.39 (5.34)	.147	130.94 (5.53)	130.46 (4.28)	.758
SNB (^{0})	74.36 (3.58)	73.86 (3.89)	.639	77.07 (3.40)	78.38 (2.07)	.158
SNPog (^{0})	75.45 (3.74)	74.78 (3.90)	.545	77.80 (3.39)	79.36 (2.21)	.097
SN/MP (^{0})	35.54 (6.54)	37.42 (4.68)	.286	32.75 (4.46)	31.31 (4.70)	.289
Gonial angle (^{0})	128.63 (7.97)	131.25 (5.59)	.226	128.68 (5.34)	126.16 (4.08)	.096
CoGo (mm)	49.76 (4.02)	47.59 (3.10)	.053	49.50 (2.49)	49.32 (2.87)	.814
ArGo (mm)	39.78 (3.40)	38.86 (3.47)	.358	40.56 (2.73)	39.76 (2.89)	.334
CoGn (mm)	99.38 (6.22)	97.42 (5.47)	.267	100.38 (4.73)	99.88 (4.46)	.719
ArGn (mm)	92.37 (5.98)	91.36 (5.53)	.556	94.37 (4.59)	93.32 (4.33)	.438
KsPog (mm)	70.21 (5.32)	68.88 (4.38)	.369	71.55 (3.71)	71.44 (4.46)	.930
GoMe (mm)	61.05 (4.83)	59.63 (5.09)	.321	62.46 (3.79)	63.05 (3.47)	.597
NMe (mm)	105.34 (5.68)	103.69 (6.01)	.330	103.87 (5.54)	100.37 (5.86)	.042
SGo (mm)	67.48 (5.54)	64.71 (4.96)	.080	68.33 (2.71)	66.44 (3.88)	.046

**mm – millimeter; ^{0} - degree*

3.3.4 Mandibular spatial position

Position of the mandible differed significantly between groups. The mandible was found retruded and at a larger inclination to the cranial base in the CG group in comparison with the NG group. In the cleft subjects, the SNB and SNPog angles were decreased and the mandibular plane angle (SN/MP) was increased. All differences were statistically significant ($p < .001$). Anterior facial height (NMe) was marginally ($p = .070$) larger in the CG group. Posterior facial height (SGo) did not differ between the groups ($p = .197$).

Comparisons of boys and girls showed only a few intergender differences. Anterior and posterior facial heights in normal boys were significantly ($p = .042$ and .046, respectively) larger than in girls. In the CG group, posterior facial height (SGo) was marginally ($p = .080$) larger in boys. SNB, SNPog, and SN/MP angles describing position of the mandible relative to the cranial base were similar in both genders ($p > .05$), except for the SNPog angle, which was marginally larger in normal girls ($p = .096$).

3.3.5 Mandibular morphology

Total length of the mandible was found to be larger in the NG group as compared with the CG group. However, *t* tests detected an intergroup difference regarding only the ArGn variable ($p = .047$).

Mandibular ramus height did not differ between groups ($p = .592$ and .169, for CoGo and ArGo, respectively). The body of the mandible was significantly longer in normal subjects as compared with individuals with cleft ($p = .050$ and .017 for KsPog and GoMe measurements, respectively). The gonial angle in CG and NG groups was similar ($p = .228$).

Intergender comparisons in the CG and NG groups showed that most measured variables were similar, except for CoGo (larger in boys; $p = .053$) in the CG group and gonial angle (more obtuse in boys; $p = .096$) in the NG group. Total mandibular length and mandibular body length did not demonstrate any intergender difference ($p > .1$).

3.4 Discussion

Our findings demonstrated that the mandible was retruded and was rotated posteriorly in the cleft group relative to individuals with ideal facial morphology. This confirms results of other investigations[7,17,20-24] that examined sagittal position of the mandible in children with complete unilateral cleft lip and palate. The common finding was a retruded mandible with increased inclination to the cranial base (posterior mandibular rotation). Mølsted et al.[7] evaluated treatment outcome in six European cleft centers and found no intercenter difference in mandibular spatial position in 9-year-old subjects with cleft. Although children without cleft were not used as controls, comparison with published cephalometric standards[25,26] indicated that the SNPog angle in children with cleft was decreased by 1.4^0 to 3.2^0 relative to children with normal facial structure. When mandibular plane inclination in subjects with cleft is contrasted with inclination in subjects without cleft, one can observe an increase of inclination of the mandibular plane to the cranial base in children with cleft, depending on the cleft center, by 1.5^0 to 4.7^0. A follow-up study[23] evaluating changes from 9 to 17 years of age confirmed that the mandible remained retrognathic with increasing inclination to the cranial base during the entire growth period. Leonard et al.[21] compared the results obtained in a Northern Ireland cleft center with the results of several European counterparts that participated in the Eurocleft program and detected similar alterations in spatial position of the mandible. Öztürk and Cura[27] found no difference in mandibular prominence in cleft versus normal groups. However, small sample size of the group might have decreased detection power so the actual difference was not detected.

Morphology of the mandible in individuals with cleft treated with one-stage repair resembled in many respects mandibular structure of controls. Although total length of the mandible was, on average, decreased in subjects with cleft, the difference was relatively small (< 2 mm) and was close to the measurement error (1.41 mm). With gonial angle and height of the ramus similar in cleft and control groups, a cause of the diminished total mandibular length was a shortened mandibular body. This finding is in agreement with the results of Swennen et al.[17]

who thoroughly evaluated mandibular structure in two cleft groups that were subjected to different surgical regimens and compared them with normal controls. They found that both cleft groups had a shorter mandibular body in comparison to normal controls, and one of the cleft groups had a decreased ramus height. Comparison of total length of the mandible from Bristol and Oslo cleft centers[28] to cephalometric norms[25,26] implied that total mandibular length in subjects with cleft was diminished by 2 to 3 mm relative to norm. However, Trotman et al.,[20] who compared primary bone-grafted with non-grafted children arrived at contradictory conclusions. They detected no intergroup difference, but the total mandibular length in children with cleft was increased by 3 to 4 mm when compared with cephalometric standards. A possible explanation for the difference between our group and the results of Trotman et al. could be the wide age range of subjects (5 to 16 years) in the latter study.

A slight decrease of mandibular body length observed in our cleft group might not have been detected if a different control group had been used. Inclusion of normal subjects, irrespective of their craniofacial structure,[17] in the control group may alter mean values of some measurements. Because Class II malocclusion caused by a small mandible is the most common skeletal malocclusion in many populations,[29-31] the inclusion of Class II subjects may decrease mean mandibular length in the control group. On the contrary, when individuals with ideal craniofacial structure are selected as controls, some comparisons to such controls may have overemphasized differences. Because we wished to use a homogeneous control group, subjects with ideal craniofacial structure were chosen. One can only speculate that if other criteria were applied during selection of the control group, no difference in mandibular body length would have been detected.

It is difficult to reconcile the finding of substantially decreased SNB and SNPog angles with an only slightly shortened mandible. A decrease of SNB or SNPog angles of 1^0 corresponds to an approximately 1.7-mm decrease of mandibular prominence. In this investigation, SNB and SNPog in children with cleft were reduced by 3^0 compared with controls. This should translate into at least 5-mm shortening of the total mandibular length. We found less than 2-mm difference in the total mandibular length. Similar findings were reported by Swennen et al.[17] This discrepancy might result from a small number of subjects in the groups, which decreased the power of the sample to detect differences in mandibular length when large variation was present. Another possible explanation is a more posterior location of the temporomandibular joints in children with cleft. Evaluation of that, however, was not part of this investigation.

The use of normal control group does not allow us to answer the question of whether disturbed mandibular morphology is the result of a one-stage surgical procedure or of diminished growth potential caused by the cleft itself. Inclusion of a group treated with a two-stage approach would help detect influence of the particular protocol on mandibular structure and position. Various modifications of treatment protocols used in local Polish hospitals prevented us from collecting a large, homogenous two-stage control group.

A sample of consecutive cases would be the most appropriate to evaluate effects of a surgical protocol. However, noncentralized treatment of children with clefts in Poland makes collection of a large sample of consecutive cases impossible. A substantial dropout rate was observed, and this is most likely due to the necessity to cover travel and accommodation expenses when coming for appointments at the Institute. Also, in our study the evaluation of mandibular morphology was carried out before the beginning of pubertal growth spurt. To draw better conclusions, further investigations are needed once craniofacial growth is complete.

3.5 References

1. Crabb JJ, Foster TD. Growth defects in unrepaired unilateral cleft lip and palate. *Oral Surg Oral Med Oral Pathol* 1977;44:329-35.
2. Morris T, Roberts C, Shaw WC. Incisal overjet as an outcome measure in unilateral cleft lip and palate management. *Cleft Palate Craniofac J* 1994;31:142-5.

3. Mars M, Plint DA, Houston WJB, Bergland O, Semb G. The Goslon Yardstick: a new system of assessing dental arch relationships in children with unilateral clefts of the lip and palate. *Cleft Palate J* 1987;24:314-22.
4. Aduss H. Craniofacial growth in complete unilateral cleft lip and palate. *Angle Orthod* 1971;41:202-13.
5. Dahl E. Transverse maxillary growth in combined cleft lip and palate. A longitudinal roentgencephalometric study by the implant method. *Cleft Palate* 1979;16:34-41.
6. Semb G. A study of facial growth in patients with bilateral cleft lip and palate treated by the Oslo CLP Team. *Cleft Palate Craniofac J* 1991;28:22-39.
7. Mølsted K, Asher-McDade C, Brattström V, Dahl E, Mars M, McWilliam J, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A Six-Centre International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 2. Craniofacial Form and Soft Tissue Profile. *Cleft Palate Craniofac J* 1992;29:398-404.
8. Mølsted K, Dahl E, Brattstrom V, McWilliam J, Semb G. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: evaluation of maxillary asymmetry. *Cleft Palate Craniofac J* 1993;30:22-8.
9. Bardach J, Roberts DM, Klausner EC. Influence of two-flap palatoplasty on facial growth in rabbits. *Cleft Palate J* 1979;16:402–11.
10. Bardach J, Dale RM, Yale R, Rosewall D, Mooney M. The influence of simultaneous cleft lip and palate repair on facial growth in rabbits. *Cleft Palate J* 1980;17:309–18.
11. Bardach J, Mooney MP. The relationship between lip pressure following lip repair and craniofacial growth: an experimental study in beagles. *Plast Reconstr Surg* 1984;73:544–55.
12. Mars M, Houston WJ. A preliminary study of facial growth and morphology in unoperated male unilateral cleft lip and palate subjects. *Cleft Palate J* 1990;27:7–10.
13. Capelozza Jr L, Taniguchi SM, da Silva Jr OG Craniofacial Morphology of adult unoperated complete unilateral cleft lip and palate patients. *Cleft Palate-Craniofacial J* 1993;30:376–81.
14. da Silva Filho OG, Normando ADC, Capelozza Filho L Mandibular growth in patients with cleft lip and/or palate – The influence of cleft type. *Am J Orthod Dentofac Orthop* 1993;104:269-75.

15. da Silva Jr. OG, Normando ADC, Capelozza Jr. L Mandibular morphology and spatial position in patients with clefts: intrinsic or iatrogenic? *Cleft Palate-Craniofacial J* 1992;29:369-75.
16. Capelozza Filho L, Normando ADC, da Silva Filho OG Isolated influences of lip and palate surgery on facial growth: comparison of operated and unoperated male adults with UCLP. *Cleft Palate-Craniofacial J* 1996;33:51–6.
17. Swennen G, Berten JL, Kramer FJ, Malevez C, De Mey A, Schwestka-Polly R, Hausamen JE. Mandibular morphology in complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2004;41:403-9.
18. Hönigmann K. One-stage closure of uni- and bilateral cleft lip and palate. *Br J Oral Maxillofac Surg* 1996;34:214-9.
19. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.
20. Trotman CA, Long RE Jr, Rosenstein SW, Murphy C, Johnston LE Jr. Comparison of facial form in primary alveolar bone-grafted and nongrafted unilateral cleft lip and palate patients: intercentre retrospective study. *Cleft Palate Craniofac J* 1996;33:91-5.
21. Leonard AG, Kneafsey B, McKenna S, Johnston CD, Burden DJ, Stevenson M. A retrospective comparison of craniofacial form in Northern Irish children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1998;35:402-7.
22. Šmahel Z, Müllerová Z, Nejedly A, Horak I. Changes in craniofacial development due to modifications of the treatment of unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1998;35:240-7.
23. Brattström V, Mølsted K, Prahl-Andersen B, Semb G, Shaw WC. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 2: craniofacial form and nasolabial appearance. *Cleft Palate Craniofac J* 2005;42:69-77.
24. Johnston CD, Leonard AG, Burden DJ, McSherry PF. A comparison of craniofacial form in Northern Irish children with unilateral cleft lip and palate treated with different primary surgical techniques. *Cleft Palate Craniofac J* 2004;41:42-6.
25. Riolo ML, Moyers RE, McNamara JA Jr, Hunter WS. An Atlas of Craniofacial Growth. Monograph no. 2, Craniofacial Growth Series. Ann Arbor, MI: Centre for Human Growth and Development; 1974.

26. Bhatia SN, Leighton BC. A Manual of Facial Growth : A Computer Analysis of Longitudinal Cephalometric Growth Data. Oxford Medical Publications by Oxford University Press, USA 1993.
27. Öztürk Y, Cura N. Examination of craniofacial morphology in children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1996;33:32-6.
28. Roberts-Harry D, Semb G, Hathorn I, Killingback N. Facial growth in patients with unilateral clefts of the lip and palate: a two-centre study. *Cleft Palate Craniofac J* 1996;33:489-93.
29. Tang EL. The prevalence of malocclusion amongst Hong Kong male dental students. *Br J Orthod* 1994;21:57-63.
30. Willems G, De Bruyne I, Verdonck A, Fieuws S, Carels C. Prevalence of dentofacial characteristics in a Belgian orthodontic population. *Clin Oral Investig* 2001;5:220-6.
31. Onyeaso CO. Prevalence of malocclusion among adolescents in Ibadan, Nigeria. *Am J Orthod Dentofacial Orthop* 2004;126:604-7.

Chapter 4

Treatment outcome after one-stage repair in children with complete unilateral cleft lip and palate assessed with the Goslon Yardstick

Piotr Fudalej
Maria Hortis-Dzierzbicka
Barbara Obloj
Dorota Miller-Drabikowska
Zofia Dudkiewicz
Anna Romanowska

Cleft Palate Craniofac J 2009;46:374-80

Summary

Purpose: To compare results of Goslon Yardstick measurement of dental arch relationships in a sample of 10-year-old Polish children with results of the Goslon measurement in published reports.

Materials and methods: Plaster models of 28 consecutively treated subjects with unilateral cleft lip and palate (UCLP) that was repaired with a one-stage simultaneous closure performed in the first year of life. All individuals were born between 1994 and 1995. The Goslon score (categories 1 to 5) was allocated. Intra- and interrater agreement was assessed with kappa statistics and Pearson correlation coefficient. Independent t tests were employed to detect difference between the score in the present and other published samples.

Results: Mean Goslon score equaled 2.44; 57% of the patients were allocated Goslon category 1 or 2, 32% were rated Goslon 3, and 11% of the patients were assigned category 4 or 5. Intrarater agreement was between 0.75 and 0.77. Interrater agreement was 0.79.

Conclusions: Dental arch relationship following one-stage repair was comparable with the results of the centers with the best outcome.

4.1 Introduction

Despite many studies attempting to establish the optimal management of a complete unilateral cleft lip and palate (UCLP), widely shared conclusions are sparse.[1] Among the questions where an agreement seems to have been reached is the effectiveness of presurgical orthopedic treatment (PSOT). It was introduced to facilitate surgical closure of the cleft through improvement of maxillary arch form. The recent results of randomized clinical trials[2-5] demonstrated no correlation between the use of PSOT and facial appearance at 18 months of age,[5] nor relationship between PSOT and occlusion in the deciduous dentition at 4 and 6 years of age.[3] Also, a view that a noncentralized treatment of children with UCLP with many low-volume surgeons involved in primary and secondary operations may produce unfavorable treatment outcome[6-8] appears to be shared by most clinicians.

Controversial issues are more abundant and regard most aspects of treatment. Timing of hard palate closure – early or delayed - is an example of such controversy. Some investigations showed better craniofacial growth after delayed repair of the hard palate;[9-11] whereas, other studies[12,13] could not find any relationship between timing of hard palate repair and midfacial growth disturbance. Increasing speech impairment, suggested to occur when delayed repair is carried out,[14,15] however, was considered not significant by other investigators.[16] Such contradictory findings make it impossible to arrive at unequivocal conclusions.

A part of the assessment of facial development in children with UCLP should be a dental arch relationship evaluation, such as performed in the large European intercenter comparison study.[6] The Goslon Yardstick[17] used in this investigation was found to be a sensitive detector of spatial discrepancy between the upper and lower dental arches.[7] Based on the dental arch relationship, five Goslon categories are allocated to a patient: from 1, suggesting an excellent treatment outcome, to 5, suggesting a very poor outcome and necessity to carry out combined orthodontic/surgical treatment. Although the Yardstick is deemed to introduce elements of subjectivity to the assessment,[18] it was frequently used in comparative studies.[19-21] The various protocols evaluated with the Goslon Yardstick ranged from two-stage closure of the cleft performed in the first year of life[19] to three-stage protocol when soft palate, lip, and hard palate were repaired at different ages.[10] There are no data, however, regarding the Goslon outcome following one-stage simultaneous repair of UCLP. Corbo et al.[22] and Savaci et al.[23] examined facial morphology in 10-year-old children subjected to one-stage surgical protocols but limited their investigation to cephalometric evaluation. Other reports[24,25] offer personal opinions as to details of surgical technique. Therefore, the purpose of this study is to assess the dental arch relationship with the Goslon Yardstick following a one-stage repair of UCLP in a sample of 28 consecutively treated 10-year-old Polish children.

4.2 Materials and methods

4.2.1 Subjects

Plaster models of 28 consecutively treated children of Polish ethnicity with a nonsyndromic complete UCLP were included to compare with published studies that evaluated dental arch relationship with the Goslon Yardstick. All subjects were born between March 1994 and December 1995 and were operated on by the same experienced surgeon (Z.D.) at the Warsaw Centre for Craniofacial Disorders, Institute of Mother and Child. The mean age at which the models were made was 10.6 years (Table 1).

Table 1 Characteristics of the cleft group.

	N	%	Age, y		
			Mean	SD	Range
Male subjects	20	71.4	10.60	0.92	8.1 - 12.2
Female subjects	8	28.6	10.73	0.83	10.0 - 12.3
Total	28		10.63	0.88	

4.2.2 Surgical management

The repair of the cleft begins with the palatal closure. Small lateral incisions are made on both sides around the maxillary tuberosities and along the posterior part of the alveolus up to the second molar region. The neurovascular palatine bundles are identified, freed by blunt dissection and mobilized. The pterygoid hamuli are always fractured, lessening the tension during the palatal repair and facilitating the medial mobilization of the velar muscle complex. The mucoperiosteal flaps are then created and elevated. The incisions along cleft margins are made in the soft and hard palate. On the larger maxillary segment, the incision on the vomer is made subperiosteally in the way to create the extended vomeric flap capable of covering the nasal floor together with the freed hard palate mucosa from the opposite side. The dorsal extension of the vomer flap will serve later to close the soft palate at the junction with the hard palate without excessive tension. The incisions along the cleft margins are then extended on both sides along the alveolus to end in the oral vestibule at the lip base. During the soft palate repair, all abnormal muscle insertions are dissected with the adhering periosteum from the posterior edge of the hard palate up to the hamuli, and the palatal muscles are sutured in the midline. A tight wound suture by the posterior alveolus without leaving any area of denuded bone ends the palatal repair. Lip repair is then performed with the use of triangular flaps by modified Tennison-Randall procedure. The most important element of our lip repair is cautious restoration of the whole nasolabial muscle complex. The proper reinsertion of the nasal wing muscles on the nasal spine is of paramount importance. The fixating sutures through the alar cartilage and nasal septum finish the procedure. No presurgical orthopedic treatment (PSOT) was carried out. Mean age when the one-stage repair was performed was 8.8 months (SD = 1.4; range = 6 to 13 months; median age = 8.8 months). In 12 children (43%), a bone grafting procedure was performed before collection of records.

4.2.3 Methods

The Review Board of the Institute of Mother and Child approved the study and informed consent was obtained.

The Goslon Yardstick[17] was used to rate dental arch relationship. The anteroposterior relationship was considered to be the most important clinically; whereas, vertical and transverse relationships helped discriminate borderline cases. According to the Goslon scale, groups 1 and 2 have occlusions that require simple orthodontic treatment; group 3 needs complex orthodontic treatment. Individuals in group 4 are at the limits of orthodontic treatment and orthognathic surgery might be indispensable; whereas, subjects in group 5 require combined orthodontic/surgical therapy.

As photographs of dental casts were demonstrated to be equivalent to plaster models,[26] sets of images (five per patient) were subsequently used to assign a Goslon score. Two raters (P.F. and B.O.) classified dental arch relationship twice each within 2 weeks. Photographs were coded and then recoded prior to the second rating, so the names of the patients remained unknown to the raters. Photographic material from the study by Mars et al.[17] was used as a reference for classification.

The Goslon scores for the Warsaw sample were subsequently compared with the published Goslon outcomes of 13 cleft centers (Table 2).

4.2.4 Statistical analysis:

Random error of the method (first versus second rating of each rater) was evaluated according to Dahlberg's[27] formula:

$$S_x = \sqrt{\frac{\Sigma D^2}{2N}}$$

with D representing the difference between corresponding first and the second Goslon classification on 28 (N) models made 2 weeks apart. Systematic error (first versus second rating) was assessed with paired *t* tests. Intra- and interobserver reliability for the casts' ratings was calculated as the Pearson correlation coefficients and proportionally weighted kappa values. Independent *t* tests were employed to compare the treatment outcomes in means of Goslon scores between the Warsaw and other cleft centers. Pearson correlation coefficient was also calculated to assess association between surgeon's caseload and the Goslon score.

Table 2 Treatment protocols of the reference cleft centers.

	A 1992	B 1992	C 1992	D 1992	E 1992	F 1992
Birth	PSOT*	No	No	PSOT	No	PSOT
2-6 mo.	Lip closure (Millard, Skoog)	Lip closure (Tennison), vomer plasty	Lip closure (various methods)	Lip closure (various methods)	Lip closure (Millard), vomer plasty	Lip closure (modified Skoog, Tennison-Randall), bone-grafting
6-12 mo.	Soft palate closure (von Langenbeck, Perko, Wardill, Kriens); 9-15 months					
12-18 mo.			Palate closure (various methods and timing)	Palate closure (various methods and timing)		Palate closure (Veau-Wardill-Kilner); at 12th month
18-24m		Palate closure (Wardill, push-back); at 22nd month			Palate closure (modified von Langenbeck); 18 - 20 months	
3-5 y.						
5-7 y.						
9-11 y.	Bone grafting; hard palate closure	Bone grafting	Bone grafting	Bone grafting	Bone grafting	Bone grafting (in case of failure of primary bone-grafting)

**PSOT = presurgical orthopedic treatment*

Table 2 Treatment protocols of the reference cleft centers – cont.

	Bristol 1996	Northern Ireland* 1998	Yorkshire 2000	Nijmegen 2005	Goteborg 2006	Tokyo 2006	Vienna 2007	Warsaw
Birth	Not reported	No (only feeding plates)	No	PSOT	Lip adhesion at 6th week	No	Lip adhesion† at 1-2 months	No
2-6 mo.	Lip closure (Millard) and alveolar surgery at 3rd month	Lip repair (Millard) and vomer plasty at 3-6 months OR lip repair (Skoog)	Lip closure (various techniques; mostly Millard)			Lip closure		
6-12 mo.	Hard and soft palate closure at 6th month			Lip closure (Millard)	Soft palate closure (push-back)		Soft palate closure (modified Gillies-Fry)	Lip, soft, and hard palate closure (one-stage)
12-18 mo.		Soft palate closure (von Langenbeck) OR palate closure (Wardill-Kilner)	Palate closure (Veau, Wardill-Kilner, von Langenbeck)	Soft palate closure (modified von Langenbeck); at 12 - 14th month	Lip and nose repair at 18 months	Palate closure within 24 months from birth		
18-24 mo.								
3-5 y.							Remainder of lip closure and nasal floor reconstruction at 4 years	
5-7 y.							Hard palate closure at 6 years	
9-11 y.		Bone grafting	Bone grafting	Bone grafting and hard palate closure (von Langenbeck)	Hard palate closure, bone grafting		Bone grafting	Bone grafting

* *Two surgeons operated on 80% patients. Two different protocols.* † *From 1990 definitive lip closure instead of lip adhesion was performed whenever possible*

4.3 Results

4.3.1 Error of the method

Random error of the method equaled 0.38 Goslon points for both raters. Systematic measurement error was not detected for either of the raters (p = 1.000 and .490 for the difference between the first and second Goslon assignment for P.F. and B.O., respectively). Intra- and interrater agreement is presented in Table 3. According to Landis and Koch,[28] kappa value greater than 0.6 represents "good" agreement, and kappa more than 0.8 indicates "very good" strength of agreement. Pearson correlation coefficient in excess of 0.7 is considered as sufficient agreement.[21]

Table 3 Intra- and interrater reliability assessed with kappa and Pearson correlation coefficients.

	Intrarater		Interrater P.F. versus B.O.	
	kappa	Pearson	Kappa	Pearson
P.F.	0.77	0.89	0.79	0.92
B.O.	0.75	0.88	—	—

4.3.2 Treatment outcome

A summary of treatment outcomes in Warsaw and 13 other cleft centers is demonstrated in Table 4. The relatively small Goslon score found in the Warsaw sample implies favorable treatment results. Only the treatment outcome of 97 subjects from Göteborg, Sweden was better (p = .005). Five more cleft centers (Vienna, Nijmegen, Eurocleft B, E, and A) achieved treatment results comparable with ours (p > .05). Seven cleft centers (Yorkshire, Northern Ireland, Eurocleft F, C, D, Tokyo, and Bristol) demonstrated statistically significant worse Goslon scores than the Warsaw sample (p < .01).

Distribution of Goslon points (Fig. 1 and Table 4) shows that 57% of individuals from the Warsaw group had favorable facial growth following a one-stage treatment protocol (Goslon 1 and 2). Only 11% of the patients demonstrated unfavorable growth of the craniofacial complex

(Goslon 4 and 5) that might require orthognathic surgery during treatment.

Table 4 Comparisons of the GOSLON score in Warsaw sample with other cleft center outcomes.

	N	Caseload/ Surgeon/ Year	Consecutive (Y or N)	Age	Goslon							Comparison *
				Mean	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	Mean	SD	p value
Sweden/ Göteborg†	97	2.2	N	10	12	74	13	1	0	2.02	0.54	0.005
Austria/Vienna	123	1.8	N	9.2	8	64	19	8	1	2.29	0.77	0.406
Netherlands/ Nijmegen	43	2	Y	9	9	52	30	9	0	2.36	0.74	0.337
Eurocleft B	27	18	Y	9	0	60	30	10	0	2.47	0.66	0.208
Eurocleft E[3]	30	6	Y	9	4	52	36	8	0	2.59	0.67	0.277
Euroceft A	24	2	Y	9	0	46	45	4	5	2.64	0.64	0.270
UK/Yorkshire	35	1.4	N	10	0	37	31	29	3	2.97	0.89	0.018
UK/Northern Ireland‡	25	2	Y	9.4	72			28		3.00	0.76	0.010
Eurocleft F	19	2.3	Y	9	0	31	37	26	6	3.03	0.75	0.006
Eurocleft C[3]	24	1.3	Y	9	5	29	29	32	5	3.04	0.87	0.003
Eurocleft D	25	1.3	Y	9	0	16	35	28	21	3.46	0.92	< 0.001
Japan/Tokyo	24	-	Y	8.3	4	4	33	55	4	3.50	0.83	< 0.001
UK/Bristol	32	3	Y	10	3	11	31	36	19	3.53	1.05	< 0.001
Poland/Warsaw	28	16	Y	10.6	14	43	32	7	4	2.44	0.96	—

** Independent t tests used. † Approximated Goslon scores read from the graph. ‡ Only combined 1+2+3 and 4+5 GOSLON scores reported*

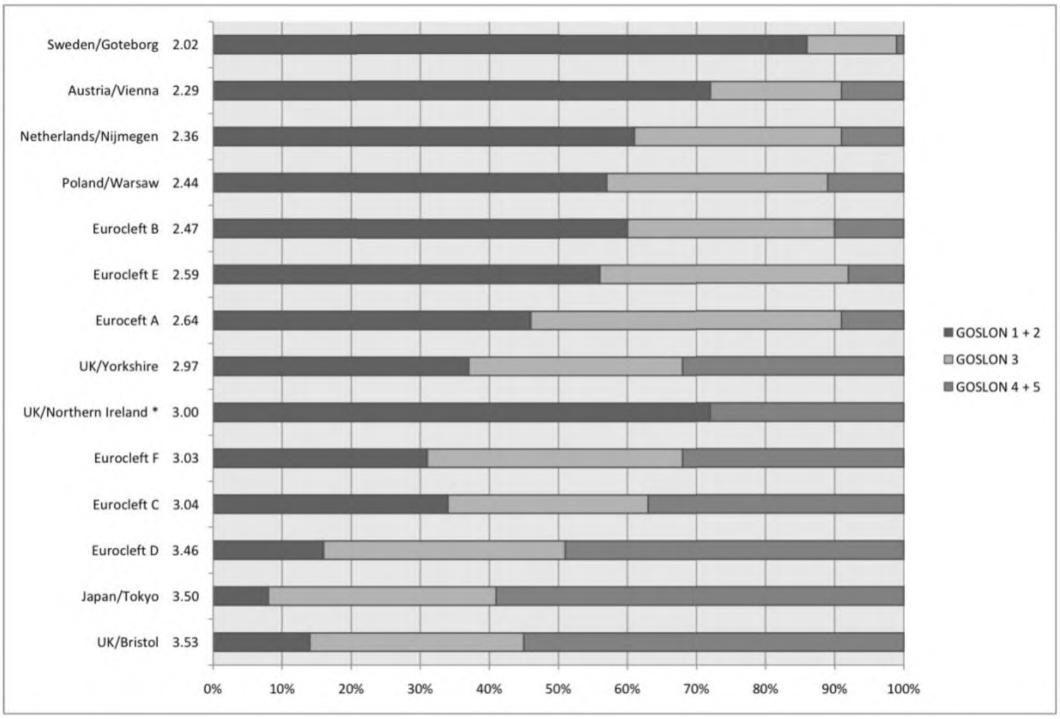


Figure 1 *Cumulative Goslon scores for various cleft centers. The horizontal axis - combined percentage of Goslon scores; the vertical axis - cleft center with mean Goslon score. The centers are ordered according to the Goslon outcome. *Only combined GOSLON 1+2+3 reported*

4.4 Discussion

A one-stage simultaneous repair of UCLP was developed at the Warsaw Centre for Craniofacial Disorders in the Institute of Mother and Child in response to previous unsatisfactory results of treatment of children with cleft. Since the first attempts to repair the cleft structures during one surgical session were undertaken more than two decades ago, the method has undergone some modifications regarding details of tissue management or timing of operation. Its most recent form has been used since May of 1993, with an average volume of 24 new patients with UCLP (including syndromic) operated on annually by one surgeon (Z.D.). Since first patients treated with the one-stage protocol now approach post-adolescence, it seemed that this is an appropriate moment to assess treatment outcome following the one-stage method.

Although advantages of participation in multicenter comparisons have often been emphasized,[6,29] it is unlikely that all cleft centers will have the opportunity to be involved in such projects. When the aim is evaluation of dental arch relationship, comparison of treatment outcome of one cleft center with published results of others with the aid of a reliable and reproducible index such as the Goslon Yardstick, seems an appropriate alternative. The Goslon system was proved to be sufficiently sensitive to discriminate between treatment results achieved at various cleft centers. Despite some subjectivity and the need to use reference models during categorization,[18] it was often used in the studies measuring outcome of the treatment of children with UCLP.[19-21,30,31]

Findings of this investigation support the general conclusion of the Eurocleft studies[32] that an association between individual elements of treatment protocol and achieved results is very weak, if any exists at all. The protocol employed in the Warsaw Cleft Centre is dissimilar to other protocols that result in comparable treatment outcomes. One-stage simultaneous repair of the UCLP performed in the first year of life was found to produce the Goslon score that approximated the results of Göteborg, Viennese, Nijmegen, and Eurocleft B, E, and A centers. However, they all used multistage surgical technique where lip repair was separated in time from palate closure. Moreover, in four centers (Göteborg, Vienna, Nijmegen, and Eurocleft A) a delayed hard palate repair at the age of 6 to 10 years was performed. In addition, the use of PSOT was inconsistent in the centers with favorable treatment outcomes. PSOT was carried out in the Eurocleft A and Nijmegen centers; whereas, the Eurocleft B, E, Viennese, Göteborg, and Warsaw cleft teams did not use it.

The simple treatment protocol performed in our cleft center resembled most closely the protocol employed in the Bristol center[19] where all cleft structures were repaired in the first year of life. In addition, a series of consecutive patients both in the Warsaw and Bristol cleft centers were operated on by one surgeon. However, the Warsaw approach differed from the Bristol protocol with regard to the number of surgical sessions required to close the cleft structures. The Bristol protocol required two sessions - lip and alveolus repair at 3 months of age followed by hard and soft palate closure at 6 months, as opposed to one operation in the Warsaw protocol. The highly significant Goslon score difference when the Bristol and Warsaw treatment outcomes are compared (2.44 versus 3.53) may result from the additional scarring due to the second operation (hard and soft palate closure) performed soon after the lip repair or, probably impossible to measure, the skill of the surgeon. The conclusions of the Eurocleft intercenter comparisons, however, implicated that distinction between the influence of different individual elements of a center's protocol on its outcome and the influence of the personnel who delivers that protocol is possible only through randomized trials carried out in the intercenter setting.[32]

The common feature of the cleft centers with more favorable treatment outcome detected in the Eurocleft study was experience of a surgeon.[7] The Eurocleft B and E centers that ranked as the best had much more centralized system with a few surgeons (i.e. one surgeon from the Eurocleft B center operated on all the patients with UCLP) performing operations. On the contrary, in the Eurocleft D center that demonstrated less advantageous outcome of the treatment, 12 operators were involved in primary and secondary surgeries of children with UCLP. Although this observation was one of the causes of the overhaul of system of care of children with a cleft in the U.K.,[8] an analysis of surgeon experience (measured as case load per person per year) in the context of the outcome of 14 cleft centers presented in this investigation does not support unequivocally correlation between experience of the operator and favorable treatment outcome. First, it is impossible to separate surgeon experience from skill. The outcome of surgeries performed by an operator with a large personal caseload but suboptimal skill may be equivalent to the results achieved by a skilled surgeon who operates on fewer patients. A "learning curve" is applicable to all operators but, likely, its course varies in different clinicians. Secondly, few new patients with UCLP treated in particular cleft centers do not allow one to verify if there is any "threshold" number of operations in a certain period of time above which quality of treatment results increases, as suggested for some other types of surgeries.[8] In general, case load per year per surgeon varied substantially among the cleft centers and ranged from one (Eurocleft C and D) to 18 (Eurocleft B), with 71% centers demonstrating fewer than three new patients operated annually by one surgeon. Three of five cleft centers that scored best, showed surgeon's personal caseload approximating two patients per year. On the other hand, the cleft centers with less advantageous Goslon scores (> 3.0 points) had rather low-volume operators with an annual caseload of three or fewer. This, along with a lack of statistically significant outcome of the Spearman rank correlation analysis ($p > .05$), suggests a rather weak relationship between yearly volume of operations and quality of treatment results.

Alveolar bone grafting was performed in 12 (43%) subjects from the cleft group; whereas, 16 (57%) children did not receive a bone graft before the time of record taking. Comparison of the Goslon score between these two subgroups did not reveal statistically significant difference. Nonparametric tests demonstrated that the dental arch relationship in both subgroups was comparable ($p = .192$). This observation is consistent with the findings of Semb,[33] Trotman et al.,[34] Daskalogiannakis and Ross,[35] Levitt et al.,[36] and Chang et al.,[37] who found that bone grafting had no adverse effect on maxillary growth.

A limitation of this investigation is the within-center assessment of dental arch relationship. Although two independent raters allocated the Goslon scores, the inclusion of an out-of-center assessor could eliminate potential bias leading to excessively optimistic conclusions regarding treatment outcome.

None of the raters participated in the training course that was recommended to ensure accuracy of assessment and optimal intra- and interrater agreement.[18] However, an interrater agreement found in the study by Susami et al.[38] where two very experienced clinicians (W.C.S. and G.S.) rated dental arch relationship and the present investigation were almost identical. This suggests that a calibration course may not be essential to warrant the correct process of the Goslon score allocation.

4.5 References

1. Kuijpers-Jagtman AM, Long Jr. RE. The influence of surgery and orthopedic treatment on maxillofacial growth and maxillary arch development in patients treated for orofacial clefts. *Cleft Palate Craniofac J* 2000;37:527-1–527-12.
2. Chan KT, Hayes C, Shusterman S, Mulliken JB, Will LA. The effects of active infant orthopedics on occlusal relationships in unilateral complete cleft lip and palate. *Cleft Palate Craniofac J* 2003;40:511-7.
3. Bongaarts CA, Kuijpers-Jagtman AM, van 't Hof MA, Prahl-Andersen B. The effect of infant orthopedics on the occlusion of the deciduous dentition in children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 2004;41:633-41.
4. Bongaarts CA, van 't Hof MA, Prahl-Andersen B, Dirks IV, Kuijpers-Jagtman AM. Infant orthopedics has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 2006;43:665-72.
5. Prahl C, Prahl-Andersen B, van 't Hof MA, Kuijpers-Jagtman AM. Infant orthopedics and facial appearance: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 2006;43:659-64.
6. Shaw WC, Asher-McDade C, Brattström V, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Semb G, The RP. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 1. Principles and study design. *Cleft Palate Craniofac J* 1992;29:393-7.
7. Shaw WC, Dahl E, Asher-McDade C, Brattström V, Mars M, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Roberts C, Semb G, The RP. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 5. General discussion and conclusions. *Cleft Palate Craniofac J* 1992;29:413-8.
8. Bearn D, Mildinhall S, Murphy T, Murray JJ, Sell D, Shaw WC, Williams AC, Sandy JR. Cleft lip and palate care in the United Kingdom--the Clinical Standards Advisory Group (CSAG) Study. Part 4: outcome comparisons, training, and conclusions. *Cleft Palate Craniofac J* 2001;38:38-43.
9. Friede H, Möller M, Lilja J, Lauritzen C, Johanson B. Facial morphology and occlusion at the stage of early mixed dentition in cleft lip and palate patients treated with delayed closure of the hard palate. *Scand J Plast Reconstr Surg Hand Surg* 1987;21:65–71.

10. Lilja J, Mars M, Elander A, Enocson L, Hagberg C, Worrell E, Batra P, Friede H. Analysis of dental arch relationships in Swedish unilateral cleft lip and palate subjects: 20-year longitudinal consecutive series treated with delayed hard palate closure. *Cleft Palate Craniofac J* 2006;43:606-11.
11. Friede H. Maxillary growth controversies after two-stage palatal repair with delayed hard palate closure in unilateral cleft lip and palate patients: perspectives from and personal experience. *Cleft Palate Craniofac J* 2007;44:129-36.
12. Noverraz AEM, Kuijpers-Jagtman AM, Mars M, van 't Hof MA. Timing of hard palate closure and dental arch relationships in unilateral cleft lip and palate patients: a mixed-longitudinal study. *Cleft Palate Craniofac J* 1993;30:391–6.
13. Stein S, Dunsche A, Gellrich NC, Harle F, Jonas I. One- or two-stage palate closure in patients with unilateral cleft lip and palate: comparing cephalometric and occlusal outcomes. *Cleft Palate Craniofac J* 2007;44:13-22.
14. Rohrich RJ, Rowsell AR, Johns DF, Drury MA, Grieg G, Watson DJ, Godfrey AM, Poole MD. Timing of hard palatal closure: a critical long-term analysis. *Plast Reconstr Surg* 1996;98:236-46.
15. Holland S, Gabbay JS, Heller JB, O'Hara C, Hurwitz D, Ford MD, Sauder AS, Bradley JP. Delayed closure of the hard palate leads to speech problems and deleterious maxillary growth. *Plast Reconstr Surg* 2007;119:1302-10.
16. Lohmander A, Friede H, Elander A, Persson C, Lilja J. Speech development in patients with unilateral cleft lip and palate treated with different delays in closure of the hard palate after early velar repair: a longitudinal perspective. *Scand J Plast Reconstr Surg Hand Surg* 2006;40:267-74.
17. Mars M, Plint DA, Houston WJ, Bergland O, Semb G. The Goslon Yardstick: a new system of assessing dental arch relationships in children with unilateral clefts of the lip and palate. *Cleft Palate J* 1987;24:314-22.
18. Mossey PA, Clark JD, Gray D. Preliminary investigation of a modified Huddart/Bodenham scoring system for assessment of maxillary arch constriction in unilateral cleft lip and palate subjects. *Eur J Orthod* 2003;25:251-7.
19. Hathorn I, Roberts-Harry D, Mars M. The Goslon yardstick applied to a consecutive series of patients with unilateral clefts of the lip and palate. *Cleft Palate Craniofac J* 1996;33:494-6.

20. Leonard AG, Kneafsey B, McKenna S, Johnston CD, Burden DJ, Stevenson M. A retrospective comparison of craniofacial form in Northern Irish children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1998;35:402-7.
21. Nollet PJ, Katsaros C, van 't Hof MA, Semb G, Shaw WC, Kuijpers-Jagtman AM. Treatment outcome after two-stage palatal closure in unilateral cleft lip and palate: a comparison with Eurocleft. *Cleft Palate Craniofac J* 2005;42:512-6.
22. Corbo M, Dujardin T, De Maertelaer V, Malevez C, Glineur R. Dentocraniofacial morphology of 21 patients with unilateral cleft lip and palate: a cephalometric study. *Cleft Palate Craniofac J* 2005;42:618-24.
23. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.
24. Lejour M. The effects of simultaneous cleft lip and palate repair on craniofacial growth. *Plast Reconstr Surg* 1989;83:751-2.
25. Hönigmann K. One-stage closure of uni- and bilateral cleft lip and palate. *Br J Oral Maxillofac Surg* 1996;34:214-9.
26. Nollet PJ, Katsaros C, van 't Hof MA, Bongaarts CA, Semb G, Shaw WC, Kuijpers-Jagtman AM. Photographs of study casts: an alternative medium for rating dental arch relationships in unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2004;41:646-50.
27. Dahlberg G. Statistical methods for medical and biological students. London: George Allen and Unwin Ltd.1940:122-32.
28. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
29. Mølsted K, Asher-McDade C, Brattström V, Dahl E, Mars M, McWilliam J, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A Six-Centre International Study of Treatment Outcome in Patients with Clefts of the Lip and Palate: Part 2. Craniofacial Form and Soft Tissue Profile. *Cleft Palate Craniofac J* 1992;29:398-404
30. Mars M, Asher-McDade C, Brattström V, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 3. Dental arch relationships. *Cleft Palate Craniofac J* 1992;29:405-8.

31. Morris DO, Roberts-Harry D, Mars M. Dental arch relationships in Yorkshire children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2000;37:453-62.
32. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93-8.
33. Semb G. Effect of alveolar bone grafting on maxillary growth in unilateral cleft lip and palate patients. *Cleft Palate J* 1988;25:288-95.
34. Trotman CA, Long RE Jr, Rosenstein SW, Murphy C, Johnston LE Jr. Comparison of facial form in primary alveolar bone-grafted and nongrafted unilateral cleft lip and palate patients: intercentre retrospective study. *Cleft Palate Craniofac J* 1996;33:91-5.
35. Daskalogiannakis J, Ross RB. Effect of alveolar bone grafting in the mixed dentition on maxillary growth in complete unilateral cleft lip and palate patients. *Cleft Palate Craniofac J* 1997;34:455-8.
36. Levitt T, Long RE Jr, Trotman CA. Maxillary growth in patients with clefts following secondary alveolar bone grafting. *Cleft Palate Craniofac J* 1999;36:398-406.
37. Chang HP, Chuang MC, Yang YH, Liu PH, Chang CH, Cheng CF, Lai JP. Maxillofacial growth in children with unilateral cleft lip and palate following secondary alveolar bone grafting: an interim evaluation. *Plast Reconstr Surg* 2005;115:687-95.
38. Susami T, Ogihara Y, Matsuzaki M, Sakiyama M, Takato T, Shaw WC, Semb G. Assessment of dental arch relationships in Japanese patients with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2006;43:96-102.
39. Sinko K, Caacbay E, Jagsch R, Turhani D, Baumann A, Mars M. The GOSLON Yardstick In Patients With UCLP: Review Of A Vienna Sample. *Cleft Palate Craniofac J* 2008;45:87-92.

Chapter 5

Dental arch relationship in children with complete unilateral cleft lip and palate following Warsaw (one-stage repair) and Oslo protocols

Piotr Fudalej
Maria Hortis-Dzierzbicka
Zofia Dudkiewicz
Gunvor Semb

Cleft Palate-Craniofac J 2009;46:648-53

Summary

Objective: To compare the dental arch relationship following one-stage repair of unilateral cleft lip and palate (UCLP) in Warsaw with a matched sample of patients treated by the Oslo Cleft Team

Material: Study models of 61 children (mean age, 11.2; SD, 1.7) with a nonsyndromic complete UCLP consecutively treated with one-stage closure of the cleft at 9.2 months (range, 6.0 to 15.8 months; SD, 2.0) by the Warsaw Cleft Team at the Institute of Mother and Child, Poland, were compared with a sample drawn from a consecutive series of patients with UCLP treated by the Oslo Cleft Team and matched for age, gender, and soft tissue band.

Methods: The study models were given random numbers to blind their origin. Four examiners rated the dental arch relationship using the GOSLON Yardstick. The strength of agreement of rating was assessed with weighted Kappa statistics. An independent t-test was carried out to compare the GOSLON scores between Warsaw and Oslo samples, and Fisher's exact tests were performed to evaluate the difference of distribution of the GOSLON scores.

Results: The intrarater and interrater agreements were high (K ≥ .800). No difference in dental arch relationship between Warsaw and Oslo groups was found (mean GOSLON score = 2.68 and 2.65 for Warsaw and Oslo samples, respectively). The distribution of the GOSLON grades was similar in both groups.

Conclusions: The dental arch relationship following one-stage repair (Warsaw protocol) was comparable with the outcome of the Oslo Cleft Team's protocol.

5.1 Introduction

The variety of protocols and surgical techniques used in the treatment of children with complete unilateral cleft lip and palate (UCLP) indicates uncertainties regarding optimal methods of treatment.[1] The Eurocleft comparison studies of outcome of six European cleft centers showed that centers with centralized care and high volume operators seemed to get better results.[2-4] Although intercenter comparison studies have their limitations (i.e. they cannot distinguish the influence of individual elements of treatment protocols on the outcome), they can demonstrate the quality of the treatment outcome achieved in a particular center in comparison with others.

All centers participating in the Eurocleft project used a multistage approach, in which more than one operation was done to close the UCLP. Although the concept of one- stage simultaneous repair of UCLP dates back to 1958,[5] few studies have so far examined the long- term outcome. In a cephalometric study, Corbo et al.[6] compared two small samples of preadolescent children with complete UCLP at 7 and 12 years of age who were operated according to the Malek procedure. In 11 children, the complete cleft was closed in one operation at 3 months of age, and in 10 children, a two-stage repair was used in which the soft palate was closed at 3 months, and the lip and hard palate closed at 6 months of age. The authors also had a control group of 10 noncleft children. No difference between the two protocols in the cleft groups was observed. Maxillary retrusion and steeper palatal plane was reported in the cleft groups compared with the noncleft group. Savaci et al.[7] reported findings from a cephalometric study of two groups of children with UCLP and one group of noncleft children. In the children with clefts, 19 subjects had had a one-stage cleft closure at a mean age of 10.2 months, and the second group, consisting of 22 subjects, had lip closure at a mean age of 4.8 months and palate closure at a mean age of 14.6 months. The follow-up in both cleft groups was performed at a mean age of 6.3 years. The authors did not find any differences in cephalometric measurements in the two cleft groups. As in many other studies, they observed retrognathic maxillo- mandibular complex, more open palatal plane, larger anterior facial height, and decreased posterior facial height in both cleft groups compared with noncleft controls. The authors concluded that their results were preliminary as the sample size was small and the follow-up short.

To the authors' knowledge, the first and only study with a long-term (10 years) multidisciplinary evaluation of outcomes in patients with UCLP following one-stage complete cleft closure (all-in-one) was published by De Mey et al. in 2006.[8] The study group consisted of 18 patients whose cleft was closed in one operation at 3 months of age. The outcomes from this group were compared with those of a group of 26 patients with UCLP operated by the Malek procedure (soft palate closure at 3 months and lip and hard palate closure at 6 months). This was a historical control study: from 1981 to 1988, the Malek procedure was used for all patients. In 1988, the all-in-one procedure was adopted for all patients. The only exclusion criterion was that the posterior cleft width was no more than 12 mm. If the cleft was wider, the patients were operated according to the Malek procedure. In the Malek cohort, two surgeons had performed most of the operations (96.2%), of which the first author (A.D.M.) had performed 42.3%. In the all-in- one cohort, one surgeon (the first author, A.D.M.) performed 88.9% of all operations. Facial growth was assessed in a cephalometric analysis. No significant difference in anteroposterior midfacial growth was found in the two cleft groups, but the one-stage procedure resulted in less downward inclination of the maxillary plane relative to the anterior cranial base compared with the cohort operated according to the Malek procedure. Early closure of the complete cleft did not have any significant benefit for the otological status or the occurrence of nasality; however, earlier intelligibility of speech was found in the all-in-one group.

Comprehensive assessment of facial growth, as in the Eurocleft studies,[3,4] should also include an evaluation of occlusion on dental study models. In some studies, the dental arch relationship was assessed by examination of the prevalence of crossbites.[9,10] Other studies have reported measurements of dental arch length and width.[11,12] In 1972, Huddart and Bodenham[13] proposed a scoring system for deciduous dentition, and Mossey et al.[14] recently adapted it to apply to the mixed dentition. Based on the degree of crossbite of individual teeth, an overall score corresponding with severity of the malocclusion was assigned to the patient. Unfortunately, lack of emphasis placed on the anteroposterior relationship of the apical bases resulted in the relatively weak ability to discriminate cases with various prognoses.

The GOSLON Yardstick was developed in 1987 by Mars et al.[15] and was found to be a simple and robust tool to assess the relationship of the maxillary and mandibular dental arches. The GOSLON Yardstick consists of five grades of dental arch relationships, ranging from 1, suggesting an excellent treatment outcome, to 5, suggesting a very poor outcome. The anteroposterior relationship was considered to be the most important clinically; whereas, vertical and transverse relationships helped discriminate borderline cases. According to the GOSLON scale, groups 1 and 2 have occlusions that require simple orthodontic treatments and group 3 needs complex orthodontic treatment. Individuals in group 4 are at the limits of orthodontic treatment, and orthognathic surgery will generally be necessary; whereas, subjects in group 5 require combined orthodontic-surgical therapy. Although the Yardstick is deemed to introduce elements of subjectivity to the assessment,[14] it has been frequently used in comparative studies.[16-21] In the Eurocleft studies, the GOSLON Yardstick was found to be a more sensitive tool in discriminating differences in outcomes of dentofacial growth in the participating centers than the cephalometric analysis of the same patients.[16,22-24]

The purpose of this study was to compare the dental arch relationship in a group of patients with UCLP following one-stage closure in Warsaw with a matched sample treated by the Oslo Cleft Team.

5.2 Material and methods

5.2.1 Subjects

The Warsaw sample consisted of plaster models of 61 consecutively treated children (42 boys, 19 girls) with a nonsyndromic complete UCLP at the Warsaw Institute of Mother and Child, Poland. All subjects in the

Polish sample were born between May 1992 and January 1996 and were operated on by the same high-volume operator (Z.D., a coauthor of this study) between May 1993 and August 1996. The mean age of the study models was 11.2 years (Table 1).

Table 1 *Sample characteristics.*

	n	%	Warsaw Age			Oslo Age		
			Mean	*SD*	*Range*	*Mean*	*SD*	*Range*
Boys	42	68.9	11.4	1.59	9.1 - 14.7	11.12	1.74	8.1 - 14.5
Girls	19	31.1	10.7	1.59	8.0 - 14.6	10.61	2.24	8.4 - 16.9
Total	61	100.0	11.18	1.65	8.0 - 14.7	10.96	1.92	8.1 - 16.9

The Oslo sample was taken from a consecutive series of patients with UCLP born between 1975 and 1980 treated by the Oslo Cleft Team (and a part of the Eurocran Good Practice Archive) and matched with the Polish sample for age, gender, and soft tissue band. Three senior surgeons had performed the first operation (lip and hard palate closure), while two additional surgeons were involved in the closure of the soft palate.

5.2.2 Surgical management

Warsaw sample. No presurgical orthopedic treatment (PSOT) was carried out. During one operation, lip, hard and soft palate were closed according to the following protocol: lip closure was undertaken using a triangular flap, and for hard palate repair, an extended vomer flap with a tight closure of the anterior palate was performed. Soft palate closure was done by dissection of all abnormal muscle insertions from the posterior margin of the hard palate up to the pterygoid hamuli, which were always fractured. The mean age at surgery was 9.2 months (SD, 2.0 months; range, 6.0 to 15.8 months). Alveolar bone grafting was performed between 9 and 12 years.

Oslo sample. No presurgical orthopedics was performed. In the first operation, the lip was closed using the Millard technique, and simultaneous hard palate closure was done using a single-layer vomer flap. The mean age for this operation was 3.3 months (range, 2.1 to 4.3

months). The soft palate was closed at a mean age of 17.2 months (range, 15.7 to 31.0 months) using a modified von Langenbeck technique. Alveolar bone grafting was performed at a mean age of 9.7 years (range, 8.8 to 12.6 years). Details of the surgical protocol can be found in Åbyholm.[25]
A summary of the Warsaw and Oslo protocols is shown in Table 2.

Table 2 Summary of treatment protocols employed in the two cleft centers PSOT – pre-surgical orthopedic treatment.

	Warsaw	Oslo
PSOT	No	No
3 months		Lip (Millard) and hard palate closure (single layer vomer flap)
6 to 12 months	Lip, soft, and hard palate closure	
18 months		Soft palate closure (modified von Langenbeck)
8 to 12 years	Alveolar bone grafting	Alveolar bone grafting

5.2.3 Methods

The Review Board of the Institute of Mother and Child approved the study.

The GOSLON Yardstick[15] was used to rate the dental arch relationship. The 122 models were coded and placed in random order. Four raters scored the models twice with the reference models present. Two of the four raters had participated in the Eurocleft studies and were experienced in using the GOSLON Yardstick.

The mean score of the first rating session was used to establish the distribution of the GOSLON groups in the samples (Fig. 1). Categorization of the groups was as follows: group 1, mean score ≤ 1.50; group 2, mean score >1.50 and ≤ 2.50; group 3, mean score >2.50 and ≤ 3.50; group 4, mean score>3.50 and ≤ 4.50; and group 5, mean score >4.50.

5.2.4 Statistical analysis

Random measurement errors (S_x) were calculated from the Dahlberg[26] equation:

$$S_x = \sqrt{\frac{\Sigma D^2}{2N}}$$

with D representing the difference between corresponding first and the second mean GOSLON score on 122 study models. Intraobserver and interobserver agreement were evaluated based on proportionally weighted Kappa statistics.[27] The interpretation of the kappa values was based on data according to Altman[28] (Table 3). An independent *t* test was carried out to compare the GOSLON scores between the Warsaw and Oslo samples, and Fisher's exact tests were performed to evaluate the difference of distribution of the GOSLON grades.

Table 3 Interpretation of Kappa values.

Kappa	*Strength of Agreement*
≤ 0.20	Poor
0.21 to 0.40	Fair
0.41 to 0.60	Moderate
0.61 to 0.80	Good
0.81 to 1.00	Very good

5.3 Results

5.3.1 Measurement error

Random measurement error was small and equaled 0.14 GOSLON points. The mean GOSLON score for the four observers varied between 2.68 and 2.69 (Warsaw sample), and 2.61 and 2.65 (Oslo sample), suggesting the absence of systematic error. Both, intrarater and interrater agreement were very good according to Altman.[28] The Kappa for intrarater concordance ranged from 0.836 to 0.974 (Table 4). The Kappa values for interrater agreement were from 0.800 (rater 1 versus 4, first rating) to 0.875 (rater 1 versus 3, second rating; Table 5).

Table 4 Intrarater agreement (weighted Kappa).

Rater	Kappa	Standard Error	95% Confidence Intervals
1	.836	.030	.777 to .894
2	.892	.024	.845 to .939
3	.866	.027	.814 to .919
4	.974	.012	.951 to .996

Table 5 Interrater agreement (weighted Kappa).

Raters	Kappa	Standard Error	95 % Confidence Intervals
First rating			
1 versus 4	.800	.030	.741 to .860
1 versus 2	.813	.031	.752 to .874
1 versus 3	.817	.029	.761 to .873
3 versus 4	.870	.027	.817 to .923
3 versus 2	.860	.028	.804 to .915
4 versus 2	.824	.030	.766 to .883
Second rating			
1 versus 4	.830	.029	.774 to .886
1 versus 2	.838	.027	.785 to .891
1 versus 3	.875	.024	.828 to .921
3 versus 4	.842	.027	.790 to .895
3 versus 2	.839	.029	.783 to .895
4 versus 2	.859	.032	.796 to .921

5.3.2 Treatment outcome

Table 6 shows the mean GOSLON scores for Warsaw (mean, 2.68) and Oslo (mean, 2.65) samples. No statistically significant difference between centers was detected (p = .795). Distribution of the GOSLON grades in both samples is demonstrated in Figure 1. In the Warsaw material, 50.8% of the sample had a score 1 or 2, 32.8% had a score 3, 14.8% had a score 4 or and only one patient had a score 5 (1.6%). In the Oslo sample 59.0% subjects scored 1 or 2, 24.6% subjects scored 3, and 14.8% scored 4 or and 1.6% scored 5. Fisher's exact tests did not show statistically significant difference between samples (p > .1).

Table 6 Intercenter comparison of the GOSLON scores.

Center	No. of subjects	Mean score	Standard Deviation	Standard Error of the mean	95% Confidence Interval for mean	Significance
Warsaw	61	2.68	0.79	0.10	2.48 to 2.89	.795
Oslo	61	2.65	0.76	0.10	2.45 to 2.84	

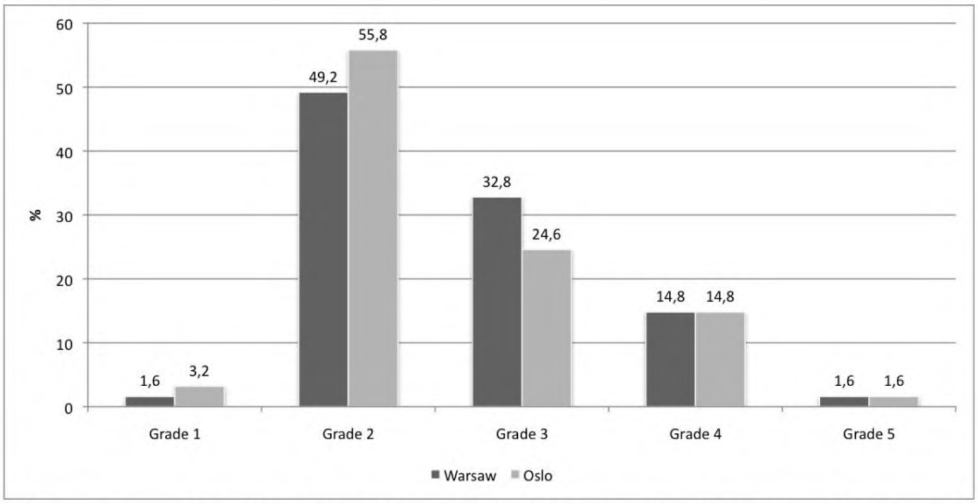


Figure 1 Distribution of the GOSLON grades in Warsaw and Oslo centers

5.4 Discussion

In this study, matching of cases was carried out to improve the equivalence of the groups compared. The extent of orthodontic treatment may have had some influence on the Goslon scores, but it was not possible to check for equivalence in the amount and timing of orthodontics since for some of the Polish patients, this information was not available.

The results of this study demonstrate that despite differences in the timing and surgical techniques used, the Warsaw and Oslo protocols produced a similar treatment outcome for the dental arch relationship. These findings support the general conclusion of the Eurocleft project[3,4] that participation of high-volume surgeons may be one of the most important factors to achieve optimal treatment outcome. The three centers with the best GOSLON score at 9 years of age in the Eurocleft study (centers A, B, and E) had high-volume operators but used different surgical protocols. Center A used PSOT, had two different lip closure techniques, the soft palate was closed at 9 to 18 months, and for most of the cohort, the closure of the hard palate was delayed until 9 years of age. Centers B and E had more similar protocols: no PSOT, the lip was closed by different techniques, and the hard palate was closed simultaneously (using a single-layer vomer flap) at 2 to 3 months of age. The soft palate was closed by different techniques between 18 and 24 months.

Treatment results comparable with the Eurocleft A, B, and E centers were found in Nijmegen,[19] Gothenburg,[20] and Vienna,[21] and these three centers also had rather different surgical protocols. PSOT was used in Nijmegen only. Although all three centers used delayed hard palate closure, lip closure was done at 4 years in Vienna (following lip adhesion at 1 to 2 months), at 6 to 12 months in Nijmegen, and at 12 to 18 months in Gothenburg (following lip adhesion performed at 6 weeks). Soft palate closure was carried out at 6 months in Gothenburg, at 6 to 12 months in Vienna, and at 12 to 18 months in Nijmegen. The hard palate closure together with alveolar bone grafting was done at 8 to 9 years in Gothenburg and Nijmegen, and in Vienna, the hard palate was closed at 6 years. The common features in these centers were rather strict adherence to the protocols and a small number of experienced operators. Less favorable treatment results detected in Eurocleft centers C and D15 and in a report on a Japanese cleft population (Susami et al., 2006) have been attributed to factors such as primary bone grafting (Eurocleft center F) and low-volume surgeons and/or decentralized treatment.

As far as the authors know, no intercenter study using the GOSLON Yardstick has been published on a sample of patients having had complete UCLP closure in one single operation. One reason for this may be that so few centers have adopted this protocol. In a survey of 201 European cleft teams, one-stage closure was used by only 5% of the teams.[30] Almost none of the literature on one-stage complete cleft closure presents objective data; although, it is claimed that this procedure is safe to do at an early age with few postoperative complications[31-33] and reduces the frequency of middle ear disease[31,32] with acceptable nasolabial appearance, speech, and facial growth.[31,32,34]

The patients in the present study with one-stage cleft closure had the surgery performed at a mean age of 9.2 months (range, 6.0 to 15.8 months). To postpone lip closure until this age is rare. In 201 European cleft teams, 47% reported to have the lip closed by 3 months, and at 6 months 92% had performed lip closure. The lip repair (part of one-stage surgery) was performed 6 months later in Warsaw than in Oslo (9 months and 3 months, respectively). It is possible that postponement of the lip closure for 9 months per se, not the surgical technique, might have been beneficial for good dental arch development.

A limitation of the intercenter comparison is that it cannot distinguish between the relationship of different elements of a center's protocol and its outcome nor between its protocols and the influence of the personnel who deliver that protocol.[4] All operations to complete the cleft closure in the Polish sample were carried out by one surgeon. Thus, it is possible that the equivalence of the dental arch relationship in the Polish sample may result from exceptional skills of the operator rather than the merits of the one-stage method. To some extent this may be clarified in the future, since from the end of the 1990s, a junior surgeon, already in training when individuals from the present sample were operated on, started one-stage repairs of the cleft.

Population distinctiveness should be considered when intercenter comparison is discussed. Studies by El-Batouti et al.[35] and Obloj et al.[36] presenting normative cephalometric data for Norwegian and Polish prepubertal children with normal occlusion demonstrated some differences between these populations. For example, maxillary and mandibular convexity (SNA and SNB angles, respectively), as well as the maxillo-mandibular relationship (ANB angle), in Norwegian 9-year-old boys was larger than in Polish 10-year-old boys. The differences ranged from 0.9u for ANB to 2.2u for SNA. Interpopulational differences for girls were less and did not exceed 1u. However, the small magnitude of differences between 9- to 10-year-old Norwegians and Poles suggests that they did not affect the GOSLON score in the studied groups. If these findings are replicated and can be generalized for other surgeons and other outcomes, the one-stage technique would have much to recommend it. The burden of care for the child and family is markedly reduced by eliminating the need for a second operation, and health care costs will be less.

5.5 Conclusions

1) The GOSLON score following one-stage repair (the Warsaw protocol) equaled 2.68 and was similar with the outcome achieved in the Oslo Cleft Centre.
2) The distribution of the GOSLON grades was comparable in the Warsaw and Oslo samples.
3) High-volume surgeons performed operations of the cleft closure in both centers.

5.6 Acknowledgments

We are grateful to Mr. Philip Eyres at the University of Manchester, United Kingdom, for his statistical analyses.

5.7 References

1. Shaw WC, Semb G, Nelson P, Brattström V, Mølsted K, Prahl-Andersen B, Gundlach KKH. The Eurocleft Project 1996-2000: overview. *J Cranio-Maxillofac Surg* 2001;29:131-40.
2. Shaw WC, Asher-McDade C, Brattström V, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Anderson B, Semb G, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 1. Principles and study design. *Cleft Palate Craniofac J* 1992;29:393–7.
3. Shaw WC, Dahl E, Asher-McDade C, Brattström V, Mars M, McWilliam J, Mølsted K, Plint DA, Prahl-Anderson B, Roberts C, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate. Part 5. General discussion and conclusions. *Cleft Palate Craniofac J* 1992;29:413–8.
4. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93–8.

5. Farina R. Total unilateral harelip: correction of severe deformity of the palate & lips in a single operation; Le Mesurier's cheiloplasty & Veau-Ernst's gnatho-urano-staphyloplasty. *Ann Chir Plast* 1958;3:199-205.
6. Corbo M, Dujardin T, de Maertelaer V, Malevez C, Glineur R. Dentocraniofacial morphology of 21 patients with unilateral cleft lip and palate: a cephalometric study. *Cleft Palate-Craniofac J* 2005;42:618-24.
7. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.
8. De Mey A, Swennen G, Malevez C, George M, Mansbach AL. Long-term follow-up of UCLP at the Reine Fabiola Children's Hospital. *B-ENT* 2006;2:44-50.
9. Pruzansky S, Aduss H. Prevalence of arch collapse and malocclusion in complete unilateral cleft lip and palate. *Eur Orthod Soc Trans* 1967;43:365–82.
10. Dahl E, Hanusardóttir B, Bergland O. A comparison of occlusions in two groups of children whose clefts were repaired by three different surgical procedures. *Cleft Palate J* 1981;17:122–7.
11. Athanasiou AE, Mazaheri M, Zarrinnia K. Dental arch dimensions in patients with unilateral cleft lip and palate. *Cleft Palate J* 1988;25:139–45.
12. Keller BG, Long RE, Gold ED, Roth MD. Maxillary dental arch dimensions following pharyngeal-flap surgery. *Cleft Palate J* 1988;25:248–57.
13. Huddart AG, Bodenham RS. The evaluation of arch form and occlusion in unilateral cleft palate subjects. *Cleft Palate J* 1972;9:194–209.
14. Mossey PA, Clark JD, Gray D. Preliminary investigation of a modified Huddart/Bodenham scoring system for assessment of maxillary arch constriction in unilateral cleft lip and palate subjects. *Eur J Orthod* 2003;25:251-7.
15. Mars M, Plint DA, Houston WJ, Bergland O, Semb G. The Goslon Yardstick: a new system of assessing dental arch relationships in children with unilateral clefts of the lip and palate. *Cleft Palate J* 1987;24:314-22.
16. Mars M, Asher-McDade C, Brattström V, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 3. Dental arch relationships. *Cleft Palate Craniofac J* 1992;29:405-8.

17. Hathorn I, Roberts-Harry D, Mars M. The Goslon yardstick applied to a consecutive series of patients with unilateral clefts of the lip and palate. *Cleft Palate Craniofac J* 1996;33:494-6.
18. Leonard AG, Kneafsey B, McKenna S, Johnston CD, Burden DJ, Stevensen M. A retrospective comparison of craniofacial form in Northern Irish Children with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1998;35:402-7.
19. Nollet PJ, Katsaros C, van 't Hof MA, Semb G, Shaw WC, Kuijpers-Jagtman AM. Treatment outcome after two-stage palatal closure in unilateral cleft lip and palate: a comparison with Eurocleft. *Cleft Palate Craniofac J* 2005;42:512-6.
20. Lilja J, Mars M, Elander A, Enocson L, Hagberg C, Worrell E, Batra P, Friede H. Analysis of dental arch relationships in Swedish unilateral cleft lip and palate subjects: 20-year longitudinal consecutive series treated with delayed hard palate closure. *Cleft Palate Craniofac J* 2006;43:606-11.
21. Sinko K, Caacbay E, Jagsch R, Turhani D, Baumann A, Mars M. The Goslon Yardstick in patients with UCLP: review of a Vienna sample. *Cleft Palate Craniofac J* 2008;45:87-92.
22. Mølsted K, Asher-McDade C, Brattström V, DahI E, McWilliam J, Mars M, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 2. Craniofacial form and soft tissue profile. *Cleft Palate-Craniofacial J* 1992;29:398-404.
23. Brattström V, Mølsted K, Prahl-Andersen B, Semb G, Shaw WC. The Eurocleft study: Intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 2: Craniofacial form and nasolabial appearance. *Cleft Palate Craniofac J* 2005;42:69-77.
24. Mølsted K, Brattström V, Prahl-Andersen B, Shaw WC, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 3: dental arch relationship. *Cleft Palate Craniofac J* 2005;42:78-82.
25. Åbyholm F. Primary closure of cleft lip and palate. In: Turvey TA, Vig KWL, Fonseca RJ, eds. Facial clefts and craniosynostosis. Philadelphia: WB Saunders C., 1996,370-83.
26. Dahlberg G. Statistical methods for medical and biological students. London: George Allen and Unwin Ltd.1940; p:122-32.
27. Fleiss JL. Statistical Methods for Rates and Proportions. New York: John Wiley & Sons; 1981:212–36.

28. Altman DG. Practical Statistics for Medical Research. London: Chapman and Hall; 1991:404–8.
29. Susami T, Ogihara Y, Matsuzaki M, Sakiyama M, Takato T, Shaw WC, Semb G. Assessment of dental arch relationships in Japanese patients with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2006;43:96-102.
30. Shaw WC, Semb G, Nelson P, Brattström V, Mølsted K, Prahl-Andersen B. The Eurocleft Project 1996-2000. Standards for care for cleft lip and palate. Amsterdam: IOS Press, 2000.
31. Kaplan I, Ben-Bassat M, Taube E, Dresner J, Nachmani A. Ten-year follow-up of simultaneous repair of cleft lip and palate in infancy. *Ann Plast Surg* 1982;8:227-8.
32. Hönigmann K. One-stage closure of uni-and bilateral cleft lip and palate. *Brit J Oral Maxillofac Surg* 1996;34:214-9.
33. Deng X, Cheng N, Wang H, Zhai J, Deng H, Pei X, Jiang J, Li F. Simultaneous repair of complete cleft lip and palate in infancy – preliminary observation (271 cases report). In Chinese. *Zhonghua Zheng Xing Wai Ke Za Zhi* 2002;18:211-3.
34. Standoli L, Cordaro L. One stage repair of unilateral complete clefts of lip and alveolus and palate. A six-year follow-up. In: Proceedings of the 7th International Congress on Cleft Palate and Related Craniofacial Anomalies. Broadbeach, Australia, 1993.
35. El-Batouti A, Øgaard B, Bishara SE. Longitudinal cephalometric standards for Norwegians between the age of 6 and 18 years. *Eur J Orthod* 1994;16:501–9.
36. Obloj B, Fudalej P, Dudkiewicz Z. Cephalometric standards for Polish 10-year-olds with normal occlusion. *Angle Orthod* 2008;78:262-9.

Chapter 6

Dental arch relationship in children with complete unilateral cleft lip and palate following one-stage and three-stage surgical protocols

Piotr Fudalej
Christos Katsaros
Catharina Bongaarts
Zofia Dudkiewicz
Anne Marie Kuijpers-Jagtman

Clin Oral Investig. 2010 May 15. [Epub ahead of print]

Summary

Objective: To compare dental arch relationship following one-stage and three-stage surgical protocols of unilateral cleft lip and palate.

Material: Dental casts of 61 children (mean age, 11.2 years; SD, 1.7), consecutively treated in one center with one-stage closure of the complete cleft at 9.2 months (SD, 2.0), were compared with a sample of 97 patients (mean age, 8.7 years; SD, 0.9), consecutively treated with a three-stage protocol including delayed hard palate closure in another center.

Methods: The dental casts were assigned random numbers to blind their origin. Four raters graded dental arch relationship and palatal morphology using the EUROCRAN index. The strength of agreement of rating was assessed with kappa statistics. Independent t tests were run to compare the EUROCRAN scores between one-stage and three-stage samples, and Fisher's exact tests were performed to evaluate differences of distribution of the EUROCRAN grades.

Results: The intra- and inter-rater agreement was moderate to very good. Dental arch relationship in the one-stage sample was less favorable than in three-stage group (mean scores, 2.58 and 1.97 for one-stage and three-stage samples, respectively; $p < 0.000$). Palatal morphology in the one-stage sample was more favorable than in the three-stage group (mean scores, 1.79 and 1.96 for one-stage and three-stage samples, respectively; $p = 0.047$).

Conclusions: The dental arch relationship following one-stage repair was less favorable than the outcome of three-stage repair. The palatal morphology following one-stage repair, however, was more favorable than the outcome of three-stage repair.

6.1 Introduction

Incomplete understanding of factors affecting outcome of treatment in children with unilateral cleft lip and palate (UCLP) has resulted in large variety of protocols and surgical techniques employed by various cleft teams worldwide. A survey of European cleft centers[1] demonstrated that 201 cleft teams practiced 194 different protocols. Although approximately 43% of them were two-stage, in which lip closure was followed by simultaneous repair of hard and soft palate, the number of primary surgeries ranged from 1 (when all cleft structures are repaired simultaneously) to 4 (when cleft structures are closed at different timings).

Comparison of treatment outcome of several European cleft centers—the Eurocleft studies—showed that one of the best treatment outcomes was achieved by a center practicing a three-stage treatment protocol with hard palate closure delayed until 8–11 years of age.[2] Nollet et al.,[3] who examined dental arch relationship in a sample of 9-year- olds treated at the Radboud University Nijmegen Medical Centre according to three-stage protocol with delayed hard palate closure (DHPC), also found a very good treatment outcome compared to the Eurocleft study. Also, studies by Lilja et al.[4] and Sinko et al.[5] revealed favorable dental arch relationships following protocols including DHPC. Lilja et al. reviewed treatment results in a sample of 104 patients treated consecutively by the Gothenburg cleft team, Sweden, and found that 85% of them were rated as having good or very good outcome. Sinko et al. examined dental arch relationship in 123 9-year-olds treated according to the Vienna concept—four-stage protocol including DHPC at 6 years—and found that 71.5% of the patients were assessed as having good or very good outcome.

Few studies have so far examined the long-term results following one-stage repair of UCLP. In a cephalometric study, Corbo et al.[6] compared two small samples of preadolescent children with complete UCLP that were operated according to the Malek procedure. In 11 children, the complete cleft was closed in one operation at 3 months of age, and in ten children, a two-stage repair was used where the soft palate was closed at 3 months and lip and hard palate closed at 6 months of age.

No difference between the two protocols was observed. Savaci et al.[7] reported cephalometric findings of two groups of children with UCLP and a non-cleft control group. In the children with clefts, 19 subjects had had a one-stage cleft closure at 10.2 months of age, and the second group consisted of 22 subjects who had lip closure at a mean age of 4.8 months and palate closure at a mean age of 14.6 months. The authors did not find any differences in cephalometric measurements between the two cleft groups at a mean age of 6.3 years. De Mey et al.[8] in a historical control study compared 18 patients with UCLP whose cleft was closed in one operation at 3 months of age with 26 patients operated according to the Malek procedure (soft palate closure at 3 months and lip and hard palate closure at 6 months). No significant difference in antero–posterior mid-facial growth was found in the two cleft groups, but the one-stage procedure resulted in less downward inclination of the maxillary plane relative to the anterior cranial base compared to the Malek cohort.

Fudalej et al.[9] evaluated in a single-center report dental arch relationship in a sample of 10-year-olds treated consecutively with one-stage approach at the Warsaw Institute of Mother and Child, Poland, and found that the outcome obtained by the Warsaw cleft team was comparable with the results of the best cleft teams. Comparison with published data, however, decreases value of evidence due to susceptibility to potential biases.[10] Intercenter comparisons offer greater transparency, hence, minimization of occurrence of some types of bias. Although intercenter studies have also their limitations, i.e., they cannot distinguish the influence of individual treatment components on the outcome, they can demonstrate the quality of the treatment outcome achieved in a particular center in comparison to others. Therefore, the purpose of this study was to perform an intercenter comparison of dental arch relationship in patients with UCLP who were treated with one-stage versus three-stage surgical treatment regimens.

6.2 Material and methods

6.2.1 Subjects

The Warsaw sample consisted of 61 children (42 males and 19 females) with a non-syndromic complete UCLP, with and without Simonart's bands, consecutively treated at the War- saw Institute of Mother and Child, Poland. All subjects were born between May 1992 and January 1996 and were operated on by the same high-volume operator (ZD) between May 1993 and August 1996. The mean age at which dental casts were made was 11.2 years (SD, 1.6; range, 9.1–14.7).

The Nijmegen sample comprised 97 consecutively treated patients with a non-syndromic complete UCLP without Simonart's bands. All patients (74 boys and 23 girls) were born between April 1976 and December 1995. The mean age at which the dental casts were made was 8.7 years (SD, 0.9; range, 7.1–11.0).

6.2.2 Surgical management

Warsaw sample. No infant orthopedic (IO) treatment was carried out. During one operation, lip, hard, and soft palate were closed according to the following protocol: lip closure was undertaken using a triangular flap; for hard palate repair, an extended vomer flap with a tight closure of the anterior palate was performed. During the soft palate repair, all abnormal muscle insertions were dissected from the posterior edge of the hard palate up to the hamuli, which were always fractured; subsequently, the palatal muscles were reconstructed and sutured in the midline. No primary nose surgery was performed at the time of operation. The mean age at surgery was 9.2 months (SD, 2.0; range, 6.0 to 15.8 months). Alveolar bone grafting was performed between 9 and 12 years.

Nijmegen sample all patients underwent IO treatment with passive plates composed of soft and hard acrylic, which were maintained until soft palate closure. No primary nose surgery was performed at the time of lip surgery. In Nijmegen, the soft palate was closed at 12–14 months of age, whereas the hard palate has been left open to be closed at the age of 9–11 years at the time of the alveolar bone- grafting procedure. For patients born before 1985, timing of hard palatal closure was variable.

For this study, only patients with closure of the hard palate after the age of 4 years were included. Summary of the Warsaw and Nijmegen protocols is shown in Table 1.

6.2.3 Orthodontic treatment

Simple orthodontic treatment, mostly with removable appliances, was performed in some children. If a subject was treated orthodontically, this was reflected in the assigned score (Table 2).

Table 1 Summary of treatment protocols used in Warsaw and Nijmegen groups.

Age	Warsaw	Nijmegen
0 - 6 months		Infant orthopedics
6 - 12 months	Lip, soft, and hard palate closure (one-stage)	Lip closure (Millard)
12 - 18 months		Soft palate closure (modified von Langenbeck); at 12 - 14th month
18 - 24 months		
9 - 11 years	Bone grafting	Bone grafting and hard palate closure (Boyne and Sands' procedure)

6.2.4 Methods

The EUROCRAN index[11] was used to rate dental arch relationship. According to the index, two components are rated separately: (1) dental arch relationship (grades from 1 to 4, when 1 means a very good treatment outcome and 4 corresponds to a poor outcome and necessity for orthognathic surgery) and (2) palatal morphology (from 1, meaning very good morphology, to 3, meaning poor morphology). Anchor models were available to illustrate the grades. A detailed description of the EUROCRAN index is given in Table 2.

The 158 models were coded and placed in random order. Four raters (PF, CK, CB, and AK) scored the models. After calibration exercises, the dental arch relationship was evaluated first. The anchor models were available through- out the calibration and the rating sessions as a reference. To evaluate intra-rater agreement, 20 randomly selected models were reassessed.

Table 2 Grade allocation according to the EUROCRAN Index.

Grades	Dental Arch Relationship	
1	(a)	Apical base relationship skeletal Class I or Class II Both central incisors positive overjet and overbite *Note: If both incisors have a positive overjet and overbite but the incisor relationship was achieved by obvious dental compensation / orthodontic treatment, the case is grade 2*
	(b)	Apical base relationship skeletal Class I or Class II No overbite but overjet markedly increased *Note: If there is no overbite and the overjet is not markedly increased, the case is grade 2*
2	Apical base relationship skeletal Class I Non-cleft incisor in positive overjet and overbite. Tilting or derotation would achieve stable positive overjet and overbite of the incisor on the cleft side *Note: the case is grade 3 if there is a moderate open bite*	
3	(a) *Class*	Apical base relationship edge-to-edge or mild Class III One or both central incisors edge-to-edge or in anterior cross-bite. Tilting or derotation would not achieve a stable positive overjet and overbite (i.e., the proclined tooth would relapse). May include moderate open bite *Note: if both incisors have an edge-to-edge relationship, but the skeletal is III, (i.e., incisor relationship was achieved by dental compensation/orthodontic treatment), the case is grade 4*
4	(a)	Apical base relationship Class III Both centrals in anterior cross-bite or one in anterior cross-bite with the other edge-to-edge. Central incisors may or may not be in contact with the lower incisors
	(b)	As grade 3 but with a marked open bite.

6.2.5 Statistical analysis

Reliability of the scorings was evaluated by calculating the intra- and inter-rater agreement with proportionally weighted kappa statistics.[12] Strength of agreement was defined according to Landis and Koch:[13] poor (kappa<0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), and very good (0.81–1.00).

Independent *t* tests were run to compare the EUROCRAN scores between Warsaw and Nijmegen samples, and Fisher's exact tests were performed to evaluate difference of distribution of the EUROCRAN grades. The level of significance was set at $p<0.05$.

6.3 Results

6.3.1 Reliability of the EUROCRAN Index

Both intra- and inter-rater agreement was moderate to very good according to Landis and Koch[13] - Tables 3 and 4. Higher values of kappa, corresponding to better agreement, were observed for the *dental arch relationship* component than for the palatal morphology component of the EUROCRAN index.

Table 2 Grade allocation according to the EUROCRAN Index – cont.

Grades	Palatal Morphology*
1	Good anterior and posterior height; minor surface irregularities (bumps and crevices); no or minor deviation of arch form
2	Moderate anterior and posterior height; Moderate surface irregularities (bumps and crevices); moderate deviation of arch form (e.g., segmental displacement)
3	Severe reduction in palate height; Severe surface irregularities (bumps and crevices); severe deviation in arch form (e.g., "hourglass" constriction).

**The worst feature of the three suggests the initial score. This may be modified up or down depending on how good the other features are. If good arch form was achieved by means of orthodontic treatment, the case is graded lower*

Table 3 Intra-rater agreement.

Raters	kappa	SE	95% CI
Dental arch relationship			
1	0.86	0.10	0.66-1.00
2	0.90	0.07	0.76-1.00
3	0.96	0.04	0.88-1.00
4	0.89	0.07	0.77-1.00
Palatal morphology			
1	0.56	0.16	0.25-0.86
2	0.91	0.09	0.72-1.00
3	0.89	0.11	0.69-1.00
4	0.64	0.17	0.30-0.97

SE standard error; CI confidence interval

Table 4 Inter-rater agreement.

Raters	kappa	SE	95% CI
Dental arch relationship			
1 vs. 2	0.73	0.04	0.65-0.80
1 vs. 3	0.73	0.04	0.66-0.80
1 vs. 4	0.77	0.03	0.71-0.84
2 vs. 3	0.73	0.03	0.66-0.79
2 vs. 4	0.81	0.03	0.75-0.87
3 vs. 4	0.70	0.04	0.63-0.77
Palatal morphology			
1 vs. 2	0.53	0.06	0.41-0.64
1 vs. 3	0.53	0.06	0.40-0.65
1 vs. 4	0.49	0.06	0.37-0.62
2 vs. 3	0.54	0.06	0.42-0.66
2 vs. 4	0.55	0.06	0.44-0.67
3 vs. 4	0.52	0.07	0.39-0.64

SE standard error, CI confidence interval

6.3.2 Treatment outcome

Tables 5 and 6 show the mean EUROCRAN scores for the Warsaw and Nijmegen samples. *Dental arch relationship* in the Warsaw group was less favorable than in the Nijmegen group (mean, 2.58 and 1.97, respectively; $p < 0.000$). On the contrary, *palatal morphology* in the Warsaw group was more favorable than in the Nijmegen group (mean, 1.79 and 1.96, respectively; $p = 0.047$).

Distribution of the EUROCRAN grades in both samples is demonstrated in Fig. 1a, b. Fisher's exact tests showed statistically significant differences between samples ($p < 0.01$).

Table 5 The mean scores for the dental arch relationship component of the EUROCRAN Index.

Group	Number	Mean	SD	SE	95% CI	*p* value
Warsaw	61	2.58	0.92	0.12	2.25-2.82	0.000
Nijmegen	97	1.97	0.88	0.09	1.79-2.15	

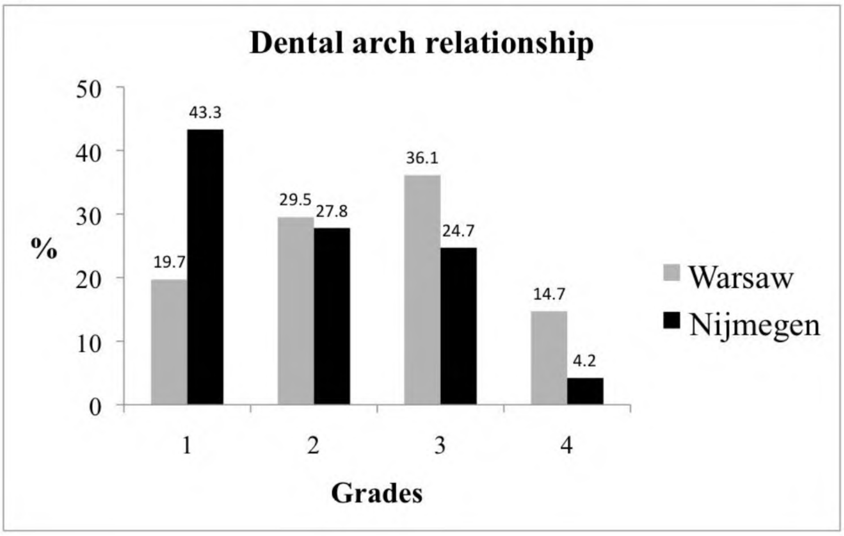
SD standard deviation, SE standard error, CI confidence interval

Table 6 The mean scores for the palatal morphology component of the EUROCRAN Index.

Group	Number	Mean	SD	SE	95% CI	*p* value
Warsaw	61	1.79	0.43	0.06	1.68-1.90	0.047
Nijmegen	97	1.96	0.55	0.06	1.85-2.07	

SD standard deviation, SE standard error, CI confidence interval

A



B

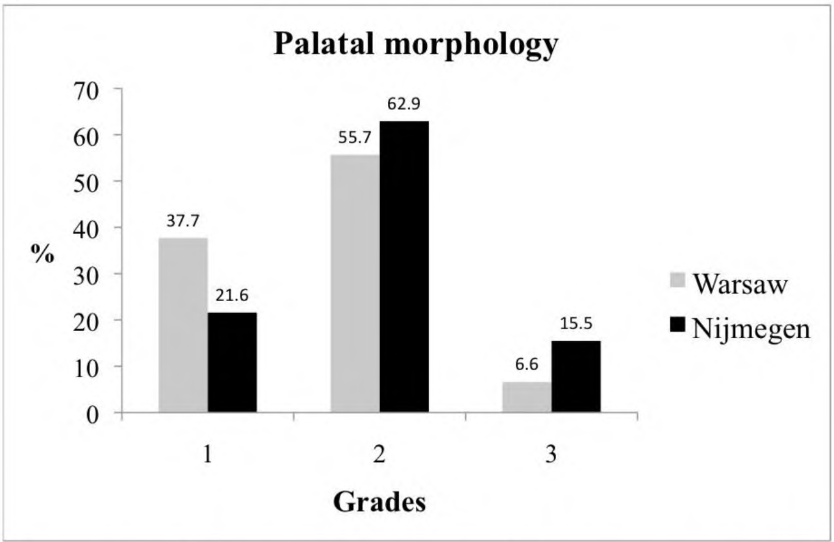


Figure 1 *Distribution of the EUROCRAN grades in Warsaw and Nijmegen groups (numbers over the bars represent percentage of distribution of the grades). a Dental arch relationship. b Palatal morphology*

6.4 Discussion

Over the last two decades, the GOSLON yardstick[14] has usually been chosen as outcome measure in studies evaluating dental arch relationship in patients with UCLP.[2,4,5,15] Since then, increasing understanding of factors adversely affecting treatment outcome resulted in an improvement of therapeutical protocols. Consequentially, differences between cleft centers became subtler, and these small differences are difficult to detect with the original GOSLON Yardstick. In response to the need for a system capable of discriminating fine differences in treatment outcomes, the EUROCRAN index was developed.[11] The index has a separate grading for dental arch relationship and palatal morphology to increase its discriminating power. Overall, the EUROCRAN index employs more detailed and nuanced guidelines for categorization of treatment outcome in comparison with the GOSLON yardstick.

The validity of the EUROCRAN index, i.e., whether the treatment outcome assessed at pre-puberty reflects the final results after completion of growth, has not been tested. However, it is recognized that a formal validation of both the EUROCRAN index and the GOSLON yardstick is not possible because it requires a sample of adults with UCLP treated only with primary surgery, for whom the dental casts made at the age of 10 years are also available.[15] Such a group likely does not exist as most patients undergo orthodontic, restorative, and bone-grafting procedures, which mask the effects of the primary surgery. Therefore, the power of the EUROCRAN index is in its face validity, which is said when the relevance of a measurement appears obvious to the investigator.[16]

Moderate to very good reliability of the EUROCRAN index, defined as the combined level of intra- and inter-rater agreement, can only be compared with reliability of the GOSLON yardstick since no studies employing the index have been published yet. The dental arch relationship component of the EUROCRAN system demonstrated satisfactory reliability - intra-rater agreement was very good, and more experienced raters (No. 1 and 2, Table 3) demonstrated similar intra-rater agreement as less experienced colleagues - and comparable with that for the GOSLON yardstick.[2,4,5] The palatal morphology component of the EUROCRAN index demonstrated a lower intra- and inter-rater agreement than the dental arch relationship component. Although values of kappa ranged from 0.49 to 0.91 (moderate to very good agreement), the lower limit of 95% confidence interval implies that agreement might have been poorer. The lower level of intra- and inter-rater agreement for palatal morphology might result from the method of scoring - among three judged elements (Table 2), the worst feature was suggestive of the final score, and this might be modified up or down depending on how good the other features were. The difference between moderate and severe deviation of arch form or minor, moderate, and severe surface irregularities is difficult to make, and therefore, anchor models need to be used as well when scoring the cleft sample. Moreover, when various features of palatal morphology showed a different degree of deviation as, for example, in the case of a severe reduction of palatal height but normal arch form, grading the case was even more difficult likely leading to the lower intra- and inter-rater agreement. It is possible that when more experience in using the EUROCRAN index will be gained, intra- and inter-rater agreement will improve, as occurred with the GOSLON yardstick in the Eurocleft study.[2,17] Overall reliability of the EUROCRAN index, however, appears acceptable.

The Warsaw one-stage and Nijmegen three-stage groups were not perfectly matched regarding age when records were taken. The Polish sample was slightly older. Since the Eurocleft studies[2] demonstrated the dental arch relationship might deteriorate with growth, it is possible that this influenced the scores. Also, inclusion of children with Simonart's bands only into the Warsaw sample might have increased inequivalence of the groups. However, long-term effects of the Simonart's band on facial development are unclear. Semb and Shaw[18] demonstrated that children with bands required fewer secondary revisions of the nose and lip. On the other hand, Johnson et al.[19] detected no relationship between the width of the cleft and dental arch relationship.

Dental arch relationship in the Warsaw group was less favorable in comparison with the Nijmegen sample, and mean difference between the groups was 0.61 EUROCRAN points on a four-grade scale. There were striking differences between the two treatment protocols. IO treatment was used only in the Nijmegen sample. Effects of IO on different aspects of facial growth and development have been recently evaluated through the randomized prospective clinical study Dutchcleft.[20-25] Findings of Dutchcleft do not substantiate claims that normalization of feeding and tongue posture with IO permits favorable growth of the maxillary segments. Conversely, it has been demonstrated that effects of IO are minimal - maxillary growth, development of occlusion, feeding, and satisfaction in motherhood were similar irrespective of use of IO. Therefore, it seems that IO was not associated with development of better dental arch relationship in the Nijmegen group in comparison with the Warsaw sample. It should be mentioned, however, that some studies,[26-28] although not using a rigorous methodology of the Dutchcleft, demonstrated a positive association between favorable facial growth and IO treatment.

Closure of a hard palate was postponed in the Nijmegen group until 8–10 years of age, whereas in the Warsaw group, the hard palate was repaired at 9 months. DHPC has been a subject of much dispute over the last decades. Although main controversy has been focused on its postulated favorable effect on maxillary growth[29,30] versus deleterious influence on speech development,[31,32] facial growth following DHPC has also been widely debated. Better facial growth after hard palate repair postponed until past-puberty was observed in the Marburg sample by Ross.[29] In the Eurocleft study, one of the three best growth and occlusal results was found in the center using DHPC.[2] Favorable dental arch relationship was also found in other cleft centers practicing DHPC - Gothenburg4 and Vienna.[5] Also, the results of the meta-analysis[33] suggest that dental arch relationship in children, whose hard palate was repaired after the age of 3, was substantially better. However, Noverraz et al.[34] and Friede et al.[35] found no difference in dental arch relationships or growth between groups of patients with different timing of hard palate repair. In a recent systematic review, Liao and Mars[36] concluded that reviewed articles did not provide firm evidence confirming favorable facial growth following DHPC. Liao and Mars implied that heterogeneity of the studies and methodological deficiencies might result in conflicting findings. Nevertheless, uncertainty of the effects of DHPC does not rule out that advantageous growth following DHPC is possible but could not have been detected due to methodological limitations. It is conceivable then that DHPC contributed to more favorable dental arch relationship found in Nijmegen three-stage group in comparison with Warsaw one-stage sample.

Mutual spatial position of apical bases and dental arches is the deciding factor during scoring with the EUROCRAN system. Maxillary morphology and position has the greatest influence on the allocation of outcome category since its growth in UCLP is often considerably disturbed. Mandibular morphology and position are usually assumed as less important. This assumption is valid when individuals from the same population are compared. However, when examined samples descend from various populations, ethnic differences in growth patterns may affect the findings. Susami et al.[37] found poorer dental arch relationship in Japanese patients in comparison with Norwegian counter- parts. They concluded that a racial difference in craniofacial growth pattern characterized by a high prevalence of mandibular prognathia (class III malocclusion) in north-eastern Asian populations might have contributed to worse rating. On the contrary, in populations where mandibular retrognathia (class II malocclusion) is more prevalent, dental arch relationship in subjects with UCLP may be more favorable. Data from studies of non-cleft[38] and UCLP subjects[39] suggest that craniofacial form in Dutch population demonstrates features conducive to occurrence of skeletal class II malocclusion. Epidemiological evidence confirms a relatively high prevalence of class II malocclusion in the Netherlands[40] and lower in Polish population.[41] Therefore, the genetic make-up of the general population might also have contributed to better dental arch relationship in Nijmegen sample.

The initial cleft size has been suggested to influence the outcome of treatment as in some studies, patients with wider clefts demonstrated poorer craniofacial growth.[42,43] To counterbalance potential inequivalence of the Warsaw and Nijmegen groups regarding initial cleft size, as not all subjects had the dental casts taken pre-surgery and the width of the cleft could not have been measured in all children, consecutively treated patients were included into the samples. This allowed obtaining equivalence of the samples as for size and severity of the cleft.[44]

The results of this investigation should be interpreted cautiously since the design of this study - intercenter comparison of treatment outcome - does not allow identification of the elements of treatment protocols responsible for a favorable or unfavorable result. This design is valuable in assessing the outcome of primary surgeries, but it does not permit to establish the key beneficial or harmful features of a specific treatment as a general conclusion.[45]

It should also be mentioned that due to problems with speech development, the surgical protocol of treatment of UCLP employed in Nijmegen has been modified. At present, a hard palate closure is performed at the age of 18 months. Therefore, DHPC is no longer practiced.

6.5 Conclusions

Based on the results of this study, the following can be concluded:

1) Dental arch relationship following a one-stage surgical protocol was worse than following a three-stage protocol.

2) Palatal morphology in a one-stage protocol was better than following a three-stage protocol; the difference, however, was likely clinically insignificant.

6.6 References

1. Shaw WC, Semb G, Nelson P, Brattström V, Mølsted K, Prahl-Andersen B. *The Eurocleft Project 1996-2000. Standards of care for cleft lip and palate in Europe.* Amsterdam: IOS Press, 2000.
2. Mølsted K, Brattström V, Prahl-Andersen B, Shaw WC, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 3: dental arch relationship. *Cleft Palate Craniofac J* 2005;42:78-82
3. Nollet PJ, Katsaros C, van 't Hof MA, Semb G, Shaw WC, Kuijpers-Jagtman AM. Treatment outcome after two-stage palatal closure in unilateral cleft lip and palate: a comparison with Eurocleft. *Cleft Palate Craniofac J* 2005;42:512-6.
4. Lilja J, Mars M, Elander A, Enocson L, Hagberg C, Worrell E, Batra P, Friede H. Analysis of dental arch relationships in Swedish unilateral cleft lip and palate subjects: 20-year longitudinal consecutive series treated with delayed hard palate closure. *Cleft Palate Craniofac J* 2006;43:606-11.

5. Sinko K, Caacbay E, Jagsch R, Turhani D, Baumann A, Mars M. The GOSLON Yardstick in patients with UCLP: review of a Vienna sample. *Cleft Palate Craniofac J* 2008;45:87-92
6. Corbo M, Dujardin T, de Maertelaer V, Malevez C, Glineur R. Dentocraniofacial morphology of 21 patients with unilateral cleft lip and palate: a cephalometric study. *Cleft Palate Craniofac J* 2005;42:618-24.
7. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.
8. De Mey A, Swennen G, Malevez C, George M, Mansbach AL. Long-term follow-up of UCLP at the Reine Fabiola Children's Hospital. *B-ENT* 2006;2:44-50.
9. Fudalej P, Hortis-Dzierzbicka M, Obłoj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z Treatment outcome after one-stage repair in children with complete unilateral cleft lip and palate assessed with the GOSLON Yardstick. *Cleft Palate-Craniofac J* 2009;46:374-80.
10. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93–8.
11. Katsaros C, Semb G, Kuijpers-Jagtman AM, Shaw BC. The Eurocran Index for dental arch relatioship and palatal development in UCLP. *Orthod Craniofac Res* submitted for publication.
12. Fleiss JL. Statistical Methods for Rates and Proportions. New York: John Wiley & Sons; 1981:212–36.
13. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159-74.
14. Mars M, Plint DA, Houston WJ, Bergland O, Semb G. The GOSLON Yardstick: a new system of assessing dental arch relationships in children with unilateral clefts of the lip and palate. *Cleft Palate J* 1987;24:314-22.
15. Atack NE, Hathorn IS, Semb G, Dowell T, Sandy JR. A new index for assessing surgical outcome in unilateral cleft lip and palate subjects aged five: reproducibility and validity. *Cleft Palate Craniofac J* 1997;34:242–1.
16. Abrahamson JH. Survey methods in community medicine. 4th edn. Churchill Livingstone, London, 1990; pp. 152–3.

17. Mars M, Asher-McDade C, Brattström V, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RPS. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: Part 3. Dental arch relationships. *Cleft Palate Craniofac J* 1992;29:405-8.
18. Semb G, Shaw WC: Simonart's band and facial growth in unilateral clefts of the lip and palate. *Cleft Palate Craniofac J* 1991;28:40-6.
19. Johnson N, Williams A, Singer S, Southall P, Sandy J. Initial cleft size does not correlate with outcome in unilateral cleft lip and palate. *Eur J Orthod* 2000;22:93-100.
20. Bongaarts CA, Kuijpers-Jagtman AM, van 't Hof MA, Prahl-Andersen B. The effect of infant orthopedics on the occlusion of the deciduous dentition in children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 2004;41:633-41.
21. Bongaarts CA, van't Hof MA, Prahl-Andersen B, Dirks IV, Kuijpers-Jagtman AM. Infant orthopedics has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 2006;43:665-72.
22. Prahl C, Kuijpers-Jagtman AM, van't Hof MA, Prahl-Andersen B. A randomised prospective clinical trial into the effect of infant orthopaedics on maxillary arch dimensions in unilateral cleft lip and palate (Dutchcleft). *Eur J Oral Sci* 2001;109:297-305.
23. Prahl C, Kuijpers-Jagtman AM, Van 't Hof MA, Prahl-Andersen B. A randomized prospective clinical trial of the effect of infant orthopedics in unilateral cleft lip and palate: prevention of collapse of the alveolar segments (Dutchcleft). *Cleft Palate Craniofac J* 2003;40:337-42.
24. Prahl C, Kuijpers-Jagtman AM, Van 't Hof MA, Prahl-Andersen B. Infant orthopedics in UCLP: effect on feeding, weight, and length: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 2005;42:171-7.
25. Prahl C, Prahl-Andersen B, Van't Hof MA, Kuijpers-Jagtman AM. Presurgical Orthopedics and Satisfaction in Motherhood: A Randomized Clinical Trial (Dutchcleft). *Cleft Palate Craniofac J* 2008;45:284-8.
26. Grabowski R, Kopp H, Stahl F, Gundlach KK. Presurgical orthopaedic treatment of newborns with clefts–functional treat- ment with long-term effects. *J Craniomaxillofac Surg* 2006;34(Suppl 2):34–44.
27. Kozelj V. Experience with presurgical nasal molding in infants with cleft lip and nose deformity. *Plast Reconstr Surg* 2007;120:738–45.

28. Barillas I, Dec W, Warren SM, Cutting CB, Grayson BH. Nasoalveolar molding improves long-term nasal symmetry in complete unilateral cleft lip-cleft palate patients. *Plast Reconstr Surg* 2009;123:1002–6.
29. Ross RB. Treatment variables affecting facial growth in complete unilateral cleft lip and palate. *Cleft Palate J* 1987;24:5-77.
30. Friede H. Maxillary growth controversies after two-stage palatal repair with delayed hard palate closure in unilateral cleft lip and palate patients: perspectives from literature and personal experience. *Cleft Palate Craniofac J* 2007;44:129-36.
31. Rohrich RJ, Rowsell AR, Johns DF, Drury MA, Grieg G, Watson DJ, Godfrey AM, Poole MD. Timing of hard palatal closure: a critical long-term analysis. *Plast Reconstr Surg* 1996;98:236-46.
32. Holland S, Gabbay JS, Heller JB, O'Hara C, Hurwitz D, Ford MD, Sauder AS, Bradley JP. Delayed closure of the hard palate leads to speech problems and deleterious maxillary growth. *Plast Reconstr Surg* 2007;119:1302-10.
33. Nollet PJ, Katsaros C, van 't Hof MA, Kuijpers-Jagtman AM. Treatment outcome in unilateral cleft lip and palate evaluated with the GOSLON Yardstick: a meta-analysis of 1236 patients. *Plast Reconstr Surg* 2005;116:1255-62.
34. Noverraz AE, Kuijpers-Jagtman AM, Mars M, van't Hof MA. Timing of hard palate closure and dental arch relationships in unilateral cleft lip and palate patients: a mixed-longitudinal study. *Cleft Palate Craniofac J* 1993;30:391-6.
35. Friede H, Priede D, Möller M, Maulina I, Lilja J, Barkane B. Comparisons of facial growth in patients with unilateral cleft lip and palate treated by different regimens for two-stage palatal repair. *Scand J Plast Reconstr Surg Hand Surg* 1999;33:73–81.
36. Liao YF, Mars M. Hard palate repair timing and facial growth in cleft lip and palate: a systematic review. *Cleft Palate Craniofac J* 2006;43:563-70.
37. Susami T, Ogihara Y, Matsuzaki M, Sakiyama M, Takato T, Shaw WC, Semb G. Assessment of dental arch relationships in Japanese patients with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2006;43:96-102.
38. Trenouth MJ, Laitung G, Naftel AJ. Differences in cephalometric reference values between five centers: relevance to the Eurocleft Study. *Br J Oral Maxillofac Surg* 1999;37:19-24.

39. Daskalogiannakis J, Dijkman GE, Kuijpers-Jagtman AM, Ross RB. Comparison of facial morphology in two populations with complete unilateral cleft lip and palate from two different centers. *Cleft Palate Craniofac J* 2006;43:471-6.
40. Burgersdijk R, Truin GJ, Frankenmolen F, Kalsbeek H, van't Hof M, Mulder J. Malocclusion and orthodontic treatment need of 15-74-year-old Dutch adults. *Community Dent Oral Epidemiol* 1991;19:64-7.
41. Śmiech-Słomkowska G. Jakościowa i ilościowa ocean zgryzu wybranej grupy dzieci [in Polish]. *Czas Stomat* 1990;43:704-7.
42. Suzuki A, Mukai Y, Ohishi M, Miyanoshita Y, Tashiro H. Relationship between cleft severity and dentocraniofacial morphology in Japanese subjects with isolated cleft palate and complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 1993;30:175–81.
43. Peltomäki T, Vendittelli BL, Grayson BH, Cutting CB, Brecht LE. Associations between severity of clefting and maxillary growth in patients with unilateral cleft lip and palate treated with infant orthopedics. *Cleft Palate Craniofac J* 2001;38:582–6.
44. Shaw WC, Dahl E, Asher-McDade C, Brattström V, Mars M, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Roberts C, The RP. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: part 5. General discussion and conclusions. *Cleft Palate Craniofac J* 1992;29:413–8.
45. Roberts CT, Semb G, Shaw WC. Strategies for the advancement of surgical methods in cleft lip and palate. *Cleft Palate Craniofac J* 1991;28:141-9.

Chapter 7

Nasolabial esthetics in children with complete unilateral cleft lip and palate after 1- versus 3-stage treatment protocols

Piotr Fudalej
Christos Katsaros
Catharina Bongaarts
Zofia Dudkiewicz
Anne Marie Kuijpers-Jagtman

J Oral Maxillofac Surg 2009;67:1661-6

Summary

Background: Facial esthetics plays an important role in social interactions. However, children with a repaired complete unilateral cleft lip and palate usually show some disfigurement of the nasolabial area. To date, few studies have assessed the nasolabial appearance after different treatment protocols. The aim of the present study was to compare the nasolabial esthetics after 1- and 3-stage treatment protocols.

Methods: Four components of the nasolabial appearance (nasal form, nasal deviation, mucocutaneous junction, and profile view) were assessed by 4 raters in 108 consecutively treated children who had undergone either 1-stage closure (Warsaw group, 41 boys and 19 girls, mean age 10.8 years, SD 2.0 yrs) or 3-stage (Nijmegen group, 30 boys and 18 girls, mean age 8.9 year, SD 0.7 yrs). A 5-grade esthetic index of Asher-McDade was used, in which grade 1 indicates the most esthetic and grade 5 the least esthetic outcome.

Results: The nasal form was judged the least esthetic in both groups and graded 3.1 (SD 1.1) and 3.2 (SD 1.1). The nasal deviation, mucocutaneous junction, and profile view were scored from 2.1 (SD 0.8) to 2.3 (SD 1.0) in both groups. The treatment outcome after the Warsaw and Nijmegen protocols was comparable. Neither overall nor any of the 4 components of the nasolabial appearance showed intercenter differences ($p > 0.1$).

Conclusions: the nasolabial appearance after the Warsaw (1-stage) and the Nijmegen (3-stage) protocols was comparable. The technique of lip repair (triangular flap in Warsaw and Millard rotation advancement in Nijmegen) gave comparable results for the esthetics of the nasolabial area.

7.1 Introduction

Physical attractiveness plays an important role in the social life and interactions of children, particularly during adolescence.[1] Usually persons who are facially attractive are preferred over unattractive ones. Both adults and children attribute positive qualities and abilities to, and behave more positively toward, attractive than unattractive individuals.[2]

Repair of the unilateral cleft lip and palate (UCLP) rarely produces ideal facial esthetics. After closure of UCLP, patients invariably demonstrate some degree of deformation of the nose and upper lip, such as nasal asymmetry, scarring of the philtral area, or an uneven mucocutaneous junction. These craniofacial impairments can result in negative psychological consequences, ranging from low self-esteem[3] to the risk of social rejection.[4]

One of the goals of the treatment of children with UCLP is to improve their esthetic appearance of structures affected by the cleft. However, the existence of a multitude of treatment protocols[5] implies a lack of agreement regarding their effectiveness and the quality of the produced outcome. Most of the studies that attempted to evaluate the long-term outcomes of treatment of UCLP have focused on cephalometric assessment of the craniofacial morphology[6,7] or dental arch relationship.[8,9] The few intercenter investigations of facial esthetics[5,10,11] could not identify specific elements of the protocols related to the nasolabial appearance. This might have resulted from the relatively small samples compared[5,12] or a comparison with the published reports.[11] Therefore, the objective of the present study was to compare the nasolabial esthetics in 2 relatively large groups of consecutive patients who had undergone different treatment protocols.

7.2 Material and methods

7.2.1 Subjects

The nasolabial appearance was rated on the frontal and profile photographs of 108 consecutively treated children with complete UCLP who were treated in 2 centers (Warsaw and Nijmegen) using 2 different surgical protocols.

A total of 60 patients from the Warsaw Centre for Craniofacial Disorders underwent 1-stage repair of all cleft structures. All operations were performed by the same surgeon (Z.D.) according to the following protocol. Lip repair was undertaken by a triangular flap; for hard palate repair, an extended vomer flap with a tight closure of the anterior palate was performed. Soft palate repair was performed by dissection of all abnormal muscle insertions from the posterior margin of the hard palate up to the pterygoid hamuli, which were always fractured; subsequently the palatal muscles were reconstructed and sutured in the midline. No infant orthopedic treatment was performed. The mean age when the 1-stage repair was performed was 9.2 months (SD 2.0; range 6 to 16). The mean age at record taking was 10.8 years (SD 2.0; range 7.4 to 15.1); 68.3% were boys and 31.7% were girls.

A total of 48 children from the Nijmegen Cleft Palate Craniofacial Centre underwent 3-stage repair. Lip closure was performed by 2 surgeons according to the Millard rotation-advancement procedure. No primary nose surgery was performed at the lip surgery. The soft palate was closed at 12 to 14 months of age (modified van Langenbeck procedure), and the hard palate was left open to be closed at the age of 9 to 11 years, together with a bone grafting procedure for the alveolar cleft (Boyne and Sands procedure). For patients who were born before 1985, the timing of hard palate closure varied. For the present study, only those patients with a 2-stage palatal closure with closure of the hard palate after the age of 4 years were included. In all patients, infant orthopedics with passive plates, composed of soft and hard acrylic, were used. The plates were maintained until soft palate closure.[13] The mean age at record taking was 8.9 years (SD 0.7; range 7.9 to 10.3); 62.5% were boys and 37.5% were girls.

7.2.2 Methods

A 5-grade esthetic index[14] was used to assess the morphology of the nasolabial area. In this index, 4 nasolabial components (ie, nasal form, nose deviation, mucocutaneous junction, and profile view) are rated separately on a 5-point scale, in which score 1 corresponds to a very good appearance, score 2 to a good appearance, score 3 to a fair appearance, score 4 to a poor appearance, and score 5 to a very poor appearance. To prevent the observers being influenced by seeing the full face, cropped frontal and profile images of the affected area were used and loaded into PowerPoint (Fig 1). Each slide consisted of the frontal and profile view of 1 patient, with a random number assigned. Four observers (P.F., A.K., C.B., and C.K.) rated all photographs. Before the rating, a calibration exercise was performed, so the raters could familiarize themselves with the rating scale.

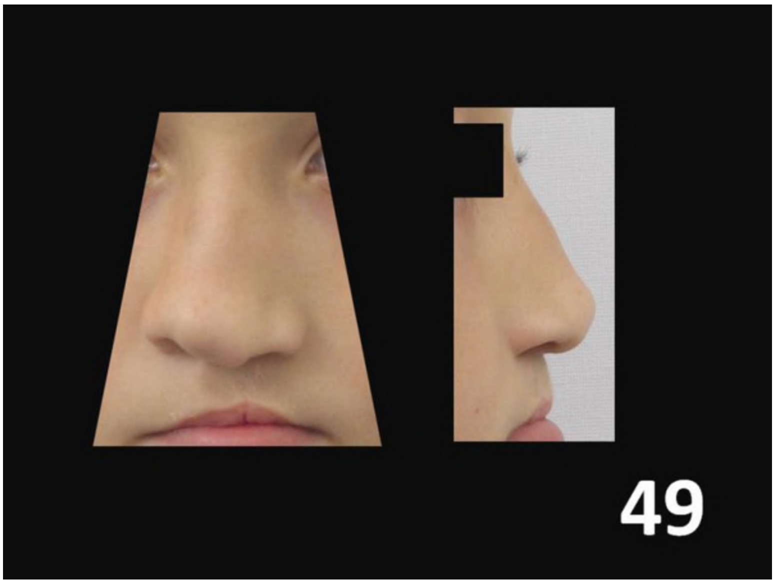


Figure 1 *Frontal and profile nasolabial view of a unilateral cleft lip and palate patient with the identifying case number for rating*

To assess intrarater reliability, 10 duplicates of War- saw and 16 duplicates of Nijmegen patients were included in a PowerPoint presentation in a random fashion. Thus, a total of 134 slides were shown during the rating session.

7.2.3 Statistical analysis

The subjective assessment of the esthetics of facial features produces considerable variation among raters.[5,14] To reduce variability, the scores for the 4 ob- servers can be averaged for each individual nasolabial component, as well as for the sum of the 4 subscores, provided the coherence among the observers is sufficient. Cronbach's alpha reliability coefficient was calculated for both the individual components and the sum of the subscores to evaluate inter-rater coherence. If the interobserver coherence was adequate, the mean scores of the 4 observers were used in the "Results" section.

The error of measurements for the mean of the panel of raters was calculated according to Dahlberg,[15] and Spearman's correlation coefficients were computed to establish the intrarater reliability.

Independent *t* tests were used to detect differences for the overall score and subscores between the Nijmegen and Warsaw groups.

7.3 Results

7.3.1 Reliability

The method error calculated according to Dahlberg was acceptable and equaled 0.45 for the overall score (range 0.43 for the nasal form to 0.49 for nasal deviation). The correlation between the first and second assessment of 26 duplicated slides was good (Table 1).

Table 1 Measurement error and correlation coefficient between duplicate measurements.

	Nasal form	Nasal deviation	Mucocutaneous junction	Profile view	Overall score
Dahlberg's measurement error	0.43	0.49	0.45	0.44	0.45
Spearman's correlation coefficient	0.82	0.63	0.76	0.82	0.81

Cronbach's alpha coefficients (Table 2) indicated good reliability for all components of the nasolabial ratings among the 4 observers. The reliability for the overall score among observers was also high (Cronbach's alpha 0.82). These data imply that the coherence among the observers was satisfactory, and the mean scores of the 4 observers are presented in the "Results" section.

Table 2 Cronbach's alpha coefficient of reliability.

	Nasal form	Nasal deviation	Mucocutaneous junction	Profile view	Overall score
Cronbach's alpha	0.81	0.69	0.77	0.84	0.82

7.3.2 Treatment outcome

Table 3 lists the results of the evaluation of the esthetics of the nasolabial area in the Warsaw and Nijmegen groups. Of the 4 components assessed, the nasal form was judged as the least esthetic in both groups (mean score 3.1, SD 1.1, and 3.2, SD 1.1, for the Warsaw and Nijmegen groups, respectively). The nasal deviation, vermilion border, and profile view were judged as relatively more esthetic, and the score ranged from 2.1 (SD 0.8) to 2.3 (SD 1.0) in both groups.

The treatment outcome after the Warsaw and Nijmegen protocols was comparable. Neither the overall nor the 4 evaluated components of the nasolabial appearance showed intercenter differences ($p > .1$).

Table 3 Comparison of the four components as well as overall nasolabial appearance between Warsaw and Nijmegen centers.

	Warsaw				Nijmegen					
	Mean score	SD	95% CI of the mean	90% Central range	Mean score	SD	95% CI of the mean	90% Central range	Diff.	*p*-value
Nasal form	3.1	1.1	2.96-3.25	1.5-4.3	3.2	1.1	3.03-3.34	1.8-4.7	0.1	0.472
Nasal deviation	2.1	0.9	1.99-2.20	1-3.3	2.1	0.8	1.95-2.18	1.3-3.2	0.0	0.680
Mucocutaneous junction	2.1	0.9	1.95-2.17	1.0-3.0	2.2	0.9	2.05-2.30	1.3-3	0.1	0.174
Profile view	2.3	1.0	2.22-2.47	1-3.8	2.3	0.9	2.13-2.39	1.3-3.5	0.0	0.379
Overall score	2.4	1.1	2.33-2.48	1.4-3.3	2.4	1.0	2.35-2.49	1.7-3.3	0.0	0.699

Diff. - Difference

7.4 Discussion

It has been recognized that an assessment of the esthetics of the areas affected by the cleft is subjective and susceptible to a large variation in the scores assigned by different raters.[10,14,16-18] Many studies have demonstrated relatively low inter-rater agreement when either professional or lay judges have evaluated facial esthetics.[17,19] Asher-

McDade et al.[14] suggested that the reliability of the assessment could be improved by replication of the measurements. The use of a panel of representative judges to generate a single mean score for each case should improve the reliability and remove the interexaminer bias. The mean score can be used, provided the coherence among the raters is substantial (i.e., the scores assigned to a group of subjects by the judges are in a similar order). Because the Cronbach's alpha coefficient of reliability implied adequate coherence,[11] we used the mean score.

The nasolabial appearance in the Warsaw and Nijmegen groups was similar despite the fundamentally different treatment protocols in the respective centers. The Warsaw protocol was simple - no infant orthopedics was used and all the cleft structures were repaired during 1 surgical session in the first year of age. The extensive Nijmegen protocol included infant orthopedics with modified Hotz's acrylic plates and 2-stage palate closure.

Originally, infant orthopedics was introduced as a method to improve the maxillary arch form and the position of the alar base to facilitate surgical repair of the lip and nose.[20,21] It was assumed that approximation of the alveolar segments before surgery would lead to reduced tension of the repaired lip and, hence, a more favorable outcome.[22] This concept had a major influence on the treatment of children with UCLP, and many of the European cleft teams adopted various forms of infant orthopedics as a part of their protocols.[12] However, Prahl et al,[23] in a randomized clinical trial (Dutchcleft) examined the effects of infant orthopedics on the facial appearance at 18 months of age and did not detect any difference between the children who had and had not undergone infant orthopedics. Nollet et al.[11] compared the nasolabial appearance in prepubertal children from the Nijmegen center and 6 "Eurocleft" centers and concluded that infant orthopedics did not provide a significant benefit for the esthetic ratings compared with centers at which no infant orthopedics was used. Our results suggesting a lack of advantage for infant orthopedics for the esthetics of the nasolabial area also agree with these investigations.[11,13,23] Therefore, it seems that infant orthopedics does not affect nasolabial esthetics, either in the short or long term.

The techniques of lip repair were different in the Warsaw (triangular flap) and Nijmegen (Millard rotation advancement) groups. As demonstrated by numerous studies,[24-26] the shape and symmetry of the nose and lip is disturbed, irrespective of the treatment protocol used. Although Schendel[27] noted that the surgical technique might affect the position of the scar in the nasolabial area, length of the reconstructed lip, or shape of Cupid's bow, direct comparisons of the outcome of the triangular flap and rotation-advancement approaches did not bring unequivocal conclusions. Cutting et al.[28] found that the principal difference between the 2 lip repairs was observed in the horizontal dimension of the nose. The position of the alar base was more normal after the Millard rotation-advancement repair, and the triangular flap repair left the alar base laterally displaced. Yamada et al.[29] concluded that the rotation-advancement method produced somewhat better results; notably the shape of the nose and nostril was more favorable. In contrast, Lazarus et al.[30] indicated that the outcome after repair using the rotation-advancement technique tended to result in an unacceptable short lip at the cleft side. Chowdri et al.[31] and Holtmann and Wray,[32] however, did not observe any major difference in the overall postoperative appearance of lip and nose between the 2 types of repair, except for the greater incidence of hypertrophic scars after the Millard rotation-advancement technique. These contrary findings could have resulted from the varying designs of the studies, which used either objective or subjective methods of assessment of the nasolabial appearance, included children who had had primary repair of the cleft at different ages (range 3 months to 3 years), followed up patients for varying periods (3 months to 18 years postoperatively), or used relatively small samples (10 to 20 patients in many investigations). This could have added to the variability of the outcomes.

The results of the present study imply that the esthetics of the nasolabial area is similar after triangular flap and rotation-advancement approaches. All 4 components (nasal form, nasal deviation, mucocutaneous junction, and profile view) did not demonstrate an intergroup difference. Our results are in accordance with the findings of Chowdri et al,[31] who compared the nasolabial appearance of 108 children with UCLP who had undergone triangular flap (n = 50; 30 children had a complete cleft) or rotation-advancement (n = 58; 38 with complete UCLP) lip repair. Although the investigators mentioned a tendency for shortening of the lip after rotation-advancement repair, no statistically significant difference between the groups was found. The relatively worse scores, such as were also reported by Chowdri et al,[31] for the nasal shape achieved in the Warsaw and Nijmegen children indicate that the nose remains a challenge to the surgeon in cleft lip and palate surgery.

The assessment of the facial esthetics was done using still images, whose limitations have been discussed previously.[11] Nonetheless, we believe their advantages, such as the ease of the collection of standardized pictures and the use of one technique allowing for the comparison of morphologic details captured at varying times, might balance the shortcomings. Although a still image is a 2-dimensional representation of a three-dimensional structure, an agreement between the facial esthetics evaluated directly and indirectly was demonstrated as moderate to good.[16] Also, a comparison of the measurements of the face performed on live subjects and digital images showed close concordance.[33] The assessment of the lip and nose esthetics on transparencies was in greater agreement with the clinical evaluation than was the 3-dimensional assessment performed using a 3-dimensional stereophotogrammetric method.[17]

The results of the present investigation should be interpreted cautiously because the Warsaw and Nijmegen groups were not perfectly matched regarding patient age when the photographs were taken. The principal reason for the lack of records at the standardized age of 9 ± 1 years was that 19 Polish subjects were either treated orthodontically at other institutions (12 children) after the primary surgical procedure and photographs were not available or they did not undergo any treatment after 1-stage repair of the cleft (7 children). Because the “Eurocleft” studies have demonstrated a tendency for the nasolabial esthetics to deteriorate with time,[12] it is possible that if the photographic records of the Polish children had been done between the ages of 8 and 10 years, the nasolabial esthetic evaluation would have produced somewhat better scores. Also, the inclusion of children with Simonart’s bands only into the Warsaw sample might have increased the inequivalence of the 2 groups. The presence of the band implies that the width of the cleft is less than when the band is absent. The long-term effects of Simonart's band on the nasolabial esthetics are unclear. Semb and Shaw[34] demonstrated only minimal differences in craniofacial growth between children with and without bands. However, children with bands required fewer secondary revisions of the nose and lip. In contrast, Nollet et al.[11] detected no relationship between the width of the cleft and nasolabial appearance.

On the basis of the results of the present study, the nasolabial appearance after the Warsaw (1-stage) and Nijmegen (3-stage) protocols was similar. Also, the technique of lip repair (triangular flap in Warsaw and Millard rotation-advancement in Nijmegen) did not seem to affect the esthetics of the nasolabial area.

7.5 References

1. Jacobsen A. Psychological aspects of dentofacial esthetics and orthognathic surgery. *Angle Orthod* 1984;54:18-35.
2. Alley TR. Social and applied aspects of perceiving faces. Hillsdale, NJ: Lawrence Erlbaum, 1988.
3. Broder H, Strauss RP. Self-concept of early primary school age children with visible or invisible defects. *Cleft Palate J* 1989;26:114-7.
4. Tobiasen JM. Social judgments of facial deformity. *Cleft Palate J* 1987;24:323-7.
5. Asher-McDade C, Brattström V, Dahl E, Asher-McDade C, Dahl E, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Semb G, Shaw WC, The RP. A six-centre international study of treatment outcome in patients with clefts of the lip and palate: part 4. Assessment of nasolabial appearance. *Cleft Palate Craniofac J* 1992;29:409-12.
6. Savaci N, Hosnuter M, Tosun Z, Demir A. Maxillofacial morphology in children with complete unilateral cleft lip and palate treated by one-stage simultaneous repair. *Plast Reconstr Surg* 2005;115:1509-17.

7. Fudalej P, Obloj B, Miller-Drabikowska D, Samarcew-Krawczak A, Dudkiewicz Z, Hortis-Dzierzbicka M. Midfacial growth in a consecutive series of preadolescent children with complete unilateral cleft lip and palate following a one-stage simultaneous repair. *Cleft Palate Craniofac J* 2008;45:667-73.
8. Lilja J, Mars M, Elander A, Enocson L, Hagberg C, Worrell E, Batra P, Friede H. Analysis of dental arch relationships in Swedish unilateral cleft lip and palate subjects: 20-year longitudinal consecutive series treated with delayed hard palate closure. *Cleft Palate Craniofac J* 2006;43:606-11.
9. Susami T, Ogihara Y, Matsuzaki M, Sakiyama M, Takato T, Shaw WC, Semb G. Assessment of dental arch relationships in Japanese patients with unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2006;43:96-102.
10. Brattström V, McWilliam J, Semb G, Larson O. Craniofacial development in children with unilateral clefts of the lip, alveolus, and palate treated according to three different regimes. Assessment of nasolabial appearance. *Scand J Plast Reconstr Surg Hand Surg* 1992;26:313-9.
11. Nollet PJPM, Kuijpers-Jagtman AM, Chatzigianni A, Semb G, Shaw WC, Bronkhorst EM, Katsaros C. Nasolabial appearance in unilateral cleft lip, alveolus and palate: a comparison with Eurocleft. *J Craniomaxillofac Surg* 2007;35:278-86.
12. Brattström V, Mølsted K, Prahl-Andersen B, Semb G, Shaw WC. The Eurocleft study: intercentre study of treatment outcome in patients with complete cleft lip and palate. Part 2: craniofacial form and nasolabial appearance. *Cleft Palate Craniofac J* 2005;42:69-77.
13. Prahl C, Kuijpers-Jagtman AM, van 't Hof MA, Prahl-Andersen B. A randomized prospective clinical trial into the effect of infant orthopedics on maxillary arch dimensions in unilateral cleft lip and palate (Dutchcleft). *Eur J Oral Sci* 2001;109:297-305.
14. Asher-McDade C, Roberts C, Shaw WC, Gallager C. Development of a method for rating nasolabial appearance in patients with clefts of the lip and palate. *Cleft Palate Craniofac J* 1991;28:385-90.
15. Dahlberg G. Statistical methods for medical and biological students. London: George Allen and Unwin Ltd., 1940. p. 122.
16. Johnson N, Sandy J. An aesthetic index for evaluation of cleft repair. *Eur J Orthod* 2003;25:243-9.

17. Al-Omari I, Millett DT, Ayoub AF, Bock M, Ray A, Dunaway D, Crampin L. An appraisal of three methods of rating facial deformity in patients with repaired complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2003;40:530-7.
18. Trotman CA, Phillips C, Essick GK, Faraway JJ, Barlow SM, Losken HW, van Aalst J, Rogers L. Functional outcomes of cleft lip surgery. Part I: Study design and surgeon ratings of lip disability and need for lip revision. *Cleft Palate Craniofac J* 2007;44:598-606.
19. Lo LJ, Wong FH, Mardini S, Chen YR, Noordhoff MS. Assessment of bilateral cleft lip nose deformity: a comparison of results as judged by cleft surgeons and laypersons. *Plast Reconstr Surg* 2002;110:733-8.
20. McNeil CK. Congenital oral deformities. *Br Dent J* 1956;18:191-8.
21. McNeil CK. Oral and Facial Deformity. London: Pitman Medical Publishers, 1954.
22. Winters JC, Hurwitz DJ. Presurgical orthopedics in the surgical management of unilateral cleft lip and palate. *Plast Reconstr Surg* 1995;95:755-64.
23. Prahl C, Prahl-Andersen B, van ’t Hof MA, Kuijpers-Jagtman AM. Infant orthopedics and facial appearance: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 2006;43:659-64.
24. Horswell BB, Pospisil OA. Nasal symmetry after primary cleft lip repair: comparison between Delaire cheilorhinoplasty and modified rotation-advancement. *J Oral Maxillofac Surg* 1995;53:1025-30.
25. Bilwatsch S, Kramer M, Haeusler G, Schuster M, Wurm J, Vairaktaris E, Neukam FW, Nkenke E. Nasolabial symmetry following Tennison-Randall lip repair: a three-dimensional approach in 10-year-old patients with unilateral clefts of lip, alveolus and palate. *J Craniomaxillofac Surg* 2006;34:253-62.
26. Reddy GS, Webb RM, Reddy RR, Reddy LV, Thomas P, Markus AF. Choice of incision for primary repair of unilateral complete cleft lip: a comparative study of outcomes in 796 patients. *Plast Reconstr Surg* 2008;121:932-40.
27. Schendel SA. Unilateral cleft lip repair- state of the art. *Cleft Palate Craniofac J* 2000;37:335-41.
28. Cutting CB, Bardach J, Pang R. A comparative study of the skin envelope of the unilateral cleft lip nose subsequent to rotation-advancement and triangular flap lip repairs. *Plast Reconstr Surg* 1989;84:409-17.

29. Yamada T, Mori Y, Minami K, Mishima K, Sugahara T. Three-dimensional facial morphology, following primary cleft lip repair using the triangular flap with or without rotation advancement. *J Craniomaxillofac Surg* 2002;30:337-42.
30. Lazarus DD, Hudson DA, van Zyl JE, Fleming AN, Fernandes D. Repair of unilateral cleft lip: a comparison of five techniques. *Ann Plast Surg* 1998;41:587-94.
31. Chowdri NA, Darzi MA, Ashraf MM. A comparative study of surgical results with rotation-advancement and triangular flap techniques in unilateral cleft lip. *Br J Plast Surg* 1990;43:551-6.
32. Holtmann B, Wray RC. A randomized comparison of triangular and rotation-advancement unilateral cleft lip repairs. *Plast Reconstr Surg* 1983;71:172-9.
33. Becker M, Svensson H, Jacobsson S. Clinical examination compared with morphometry of digital photographs for evaluation of repaired cleft lips. *Scand J Plast Reconstr Surg Hand Surg* 1998;32:301-6.
34. Semb G, Shaw WC. Simonart's band and facial growth in unilateral clefts of the lip and palate. *Cleft Palate Craniofac J* 1991;28:40-6.

Chapter 8

General discussion

8.1 Introduction

The objective of the current thesis was to evaluate long-term outcomes of the Warsaw treatment protocol based on a one-stage surgical repair of complete unilateral cleft lip and palate (UCLP). The rationale for performing a one-stage closure of the complete cleft in the lip and palate ranges from a better speech development to a decreased cost of treatment and less burden of care. Provided that facial growth and esthetics are not adversely affected by a one-stage approach, this treatment protocol might have much to recommend for.

Cleft centers rarely use this type of surgical protocol and only limited data regarding its effectiveness are available. The central question investigated here was growth and esthetics of the face following one-stage simultaneous repair of the lip and palate in UCLP performed in the 1st year of life. We aimed to find out whether morphology of the maxillofacial complex, dental arch relationship, and nasolabial appearance in 10-year-old children treated with the one-stage repair were comparable with the outcomes obtained by leading centers using multi-stage surgical protocols. To this end, we compared craniofacial morphology of children with UCLP with that of noncleft controls originating from the Polish population[1,2] (Chapter 2 and 3). Subsequently, we evaluated dental arch relationship as a single center study in comparison to the published data of the Eurocleft and other cleft centers[3] (Chapter 4). Finally, the results achieved in the Warsaw Cleft Centre with respect to dental arch relationship and nasolabial appearance were compared in an international setting with the outcome of the Oslo Cleft Centre, practicing two-stage treatment protocol[4] (Chapter 5), and the outcome of the Nijmegen Cleft Palate Craniofacial Unit, employing three-stage protocol with delayed hard palate closure[5,6] (Chapter 6 and 7)

It should be realized, however, that assessment of speech must be carried out to have a complete picture of effectiveness of the one-stage protocol. Although speech evaluation was not included into the current thesis due to missing records for many patients, it is planned in the nearest future.

8.2 Methodological considerations

In this thesis, it was encountered that reliable assessment of the treatment outcome and comparison with published reports, was hindered by medium to low level quality of study designs in clinical cleft research, by inconsistencies between various outcomes found in the same sample, and, also, by potential influence of ethnic growth patterns on the compared results.

8.2.1 Study design

During the past years, there has been an increasing understanding that progress in surgery depends also on adoption of the principles of evidence-based medicine, which may be defined as ... *use of current best evidence in making decisions about the care of the individual patient.*[7] The concept of best evidence has been formalized and a hierarchy of sources of evidence has been widely accepted. For example, the Centre for Evidence Based Medicine (CEBM) of the University of Oxford[8] that developed the hierarchy of evidence, ranking the quality of scientific evidence from 1 (highest) to 5 (lowest), where grade 1 corresponds with systematic review of RCTs (1a) or individual RCT with narrow confidence interval (1b), grade 2 – with systematic review of cohort studies (2a), individual cohort study and low quality RCT (2b), and outcomes research (2c), grade 3 – with systematic review of case-control studies (3a) and individual case-control study (3b), grade 4 – with case-series (and poor quality cohort and case-control studies), and grade 5 – with expert opinion without explicit critical appraisal. According to the U.S. Preventive Services Task Force[9] - an independent panel of experts that systematically reviews the evidence of effectiveness of various therapeutical modalities and develops recommendations for their clinical use - the highest level in a hierarchy of research designs have (I) a properly powered and conducted randomized controlled trial (RCT) or well-conducted systematic review or meta-analysis of homogeneous RCTs; the intermediate level in a hierarchy occupies (II-1) a well-designed controlled trial without randomization, (II-2) a well-designed cohort or case-control analytic study, and (II-3) a multiple time series with or without the intervention and/or uncontrolled experiments with dramatic results; whereas, the lowest level in a hierarchy of study design occupy (III) opinions of respected authorities, based on clinical experience, descriptive studies or case reports, and reports of expert committees. Thus there is complete agreement that RCTs and systematic reviews of RCTs provide best scientific evidence, and expert opinions constitute the weakest evidence.

An RCT is preferred because only this study design allows conclusions on cause and effect relationships of a particular surgical technique and outcome. The advantage of an RCT is that compared groups are balanced regarding various types of biases, both known and unknown factors influencing the outcome. Furthermore, concealment of random allocation and blinding of investigators and patients to the type of intervention, guard against additional bias. Consequently, if a treatment effect is observed, there will be more confidence in concluding that one intervention is better than the other. Moreover, well-designed RCTs have high internal validity and good generalizability, i.e. their results may be extrapolated beyond the study group to general population.[10,11]

However, RCTs in surgery are performed relatively rarely in comparison with other medical fields,[12] which implies that most surgical investigations have a lower level of evidence than non-surgical studies. In surgical trials it is more difficult to obtain randomization of patients and concealment of treatment modality to the investigator than in non-surgical trials. RCTs in rare anomalies such as cleft lip and palate, are even more challenging because small trial populations demand involvement of many centers in a single RCT. A need for multiple-site coordination, difficulty to recruit a sufficient number of participants in a reasonable period of time, involvement of many different surgeons, lack of clinical equipoise, the length of follow-up, costs involved, and ethics of consent for babies in randomized clinical trials cause that the vast majority of evidence in the cleft lip and palate field comes from retrospective studies.

Although retrospective studies do not provide the highest level of evidence, they are useful in the clinical audit. This may be defined as

...the systematic critical analysis of the quality of care including procedures for diagnosis and treatment, the use of resources, and the resulting outcome and quality of life for the patient.[13] The main objective of a clinical audit is thus improvement of delivered health care through a continuous cycle of 1) establishing best practice, 2) measuring care against established criteria, 3) taking action to improve care, and 4) monitoring to sustain improvement. In the cleft lip and palate field a good practice archive and outcome criteria were established in a series of Eurocleft studies.[14] As mentioned previously, the current thesis aimed to measure the outcomes obtained in the Warsaw Cleft Centre against the outcomes of other cleft centers that had been found to be achieving favorable results. And indeed, both cephalometric assessment of facial morphology and comparison with published data, as well as inter-center comparisons of dental arch relationship and nasolabial esthetics were intended to allow the Warsaw team to evaluate the relative success of its protocol and to take remedial action, if shortcomings were identified. It was reassuring to find out that the Warsaw Cleft Centre achieved outcomes in the mainstream of competent practice. Therefore, the clinical audit revealed that, for the ages and outcomes assessed, no immediate improvement of the Warsaw protocol is required.

8.2.2 Single center versus inter-center research

Single center reports are still a very common type of research in the cleft and lip field. Despite their popularity they are susceptible to various biases that can reduce the validity of the conclusions. Some biases, however, may be minimized when inter-center comparisons are carried out.[14] In Chapter 4, the treatment outcome after one-stage repair was demonstrated as a single center report.[3] Dental arch relationship of 28 consecutively treated children (they were subsequently included into the consecutive 61-subject sample assessed in Chapter 5, 6, and 7[4,5,6]) was evaluated with the GOSLON Yardstick by two assessors from the Warsaw Cleft Centre; no external assessor participated in the evaluation. The results of the assessment (mean GOSLON score was 2.44 points, SD = 0.96) differed from the results of a comparable evaluation, which, however, was performed by four assessors, including three external ones (mean GOSLON score was 2.68 points, SD = 0.79; Chapter 5[4]). Although it is possible that the 28-subject subgroup showed better dental arch relationships than the entire 61-subject group, it is more likely that the absence of experienced external assessors and the lack of calibration exercises, resulted in overly optimistic rating. This situation should be cautionary for future research, as well as during interpretation of the findings of other single center reports.

8.2.3 Evaluation of surgical intervention

A surgical intervention is a complex procedure delivered by a surgeon and is affected by characteristics such as knowledge, skill, and personal preferences of an operator. The delivery of a surgical intervention also depends on the other members of the team (anesthetists, nurses) and pre-operative and post-operative care (emergency department, imaging services, postoperative recovery ward, intensive care, and rehabilitation programs). All these factors may favorably or unfavorably influence the outcome.[10,11]

The skill of the operator has often been emphasized as an important, yet extremely difficult to measure, element affecting the outcome of surgical intervention.[11,12] Proficiency of the surgeon is often equated with experience, i.e. it is thought to be associated with the number of performed operations of a particular type in a given period of time. In this thesis, the same experienced surgeon operated on all evaluated patients. One should bear in mind that exceptional skill of the operator rather than a one-stage repair, could be the key factor influencing the outcome of treatment. However, the relationship between surgeon's experience and long-term treatment outcome is unclear. Although the conclusion of the Eurocleft study was that favorable treatment results of the cleft center were associated with participation of few surgeons with a large personal caseload, Bearn et al.[15] demonstrated that a high volume of operations was not necessarily associated with high quality. Of seven operators who carried out 5 or more repairs of UCLP per year and classified as high-volume surgeons in the Clinical Standards Advisory Group (CSAG) study, four operators provided results that showed beneficial effects of volume on dentofacial outcomes, but the other three did not. Moreover, not all outcomes were equally affected by the type of operator (high-volume versus low-volume). For example, speech production (i.e. intelligibility or absence of hypernasality) or nasal appearance were more favorable following cleft repair performed by an experienced surgeon, but dental relationship or profile appearance did not seem to be related to surgeon's experience. Notwithstanding these conflicting findings, a surgeon's skill should be regarded as a factor, which might significantly influence the therapeutical results.

In this dissertation, evaluation of facial morphology, dental arch relationship, and nasolabial esthetics were used to assess the effect of surgical intervention. These variables, although important and related with intervention, are indirect measures of the surgical result. A complete picture of the effectiveness of the one-stage treatment protocol should also include information regarding surgical complications such as fistula rate or number of revision surgeries, length of hospital stay during the entire period of treatment, etc. These data help to quantify the burden of care imposed by the Warsaw protocol. We did not include evaluation of burden of care for a fundamental reason – all the evaluated subjects were at least several years before completion of treatment. During the following years patients might be treated orthodontically with variable intensity, might need a revision surgery or might require othognathic surgery. All these factors influence the burden of care. Therefore, we decided to assess burden of care in our cohort once orthodontic/surgical treatment is complete.

8.2.4 Methods to assess facial morphology, dental arch relationship and nasolabial appearance

Recently, visualization techniques have been evolving rapidly and two-dimensional (2D) techniques are being gradually replaced by three-dimensional (3D) technology, which offers new possibilities of registration of three tissue groups: facial soft tissues, facial skeleton, and the dentition, frequently referred to as a triad.[16] A cone beam computed tomography (CBCT) makes accurate imaging of the hard tissues of the face possible with a relatively low radiation dose. It was also demonstrated that conventional cephalometric radiographs could be compared with constructed cephalometric radiographs from CBCT scans and the latter can be used for longitudinal research.[17] 3D photography enables to capture textured surfaces of the face that are photorealistic in appearance. Moreover, it makes evaluation of volumetric changes of the face possible during growth and/or treatment. Digital dental models are, in turn, easy to store and retrieve. They can be manipulated in all planes of space, sectioned in any plane and measured along any plane. The virtual images can be sent worldwide for consultation, for Internet study groups or research purposes. In addition, they allow fusion of all tissue groups of the triad into a "3D virtual head". All these 3D techniques enhance complex treatment planning in patients with cleft anomaly and are useful in assessment of treatment results.

In the present cohort treatment outcome was evaluated mostly on the basis of 2D cephalometry and photography. The only 3D records here were plaster dental casts. This resulted from an unavailability of 3D alternatives when the assessment of the subjects from the Warsaw Cleft Centre was initiated. Two-dimensional cephalometry has been the most common type of outcome assessment of craniofacial morphology in cleft lip and palate research. However, although cephalometry has been utilized since the 1930's, it has never been possible to arrive at a universally accepted cephalometric analysis. For example, definitions of cephalometric landmarks may differ; thus, comparison of two measurements based on differently defined landmarks can be misleading. When linear measurements are to be compared, information regarding magnification is essential, but this is not always available, even in studies presenting normative data.[18] This means that cephalometric analysis is quite often limited to angular measurements and ratio variables, which are not affected by an unknown magnification factor. Moreover, conventional cephalometrics is not the optimal diagnostic tool in patients presenting with multi-dimensional growth impairment because it is not capable of visualization of transverse growth problems. Extra-oral still photographs have, in turn, relatively poor ability to capture correct geometry of the soft tissue surface of the face and do not display facial animation. While being conscious of these limitations, important advantages of 2D cephalometry and photography seem to offset some of these shortcomings. Although there is no doubt that in the near future 3D techniques will become a routine method in planning and evaluation treatment outcome in patients with orofacial clefts, a relative novelty, a lack of standardization, high costs, and a moderate availability of this method cause that performing a clinical audit on the basis of 3D records would likely be impossible at the moment.

8.2.5 Ethnic differences

An important challenge in drawing conclusions of the present study is the presence of conflicting results following assessment of different elements of facial morphology. For example, it was found that maxillary prominence evaluated cephalometrically in the children from the Warsaw group was comparable with that in the Nijmegen group;[19] but the same maxillary prominence seemed significantly less pronounced when judged on the basis of examination of dental arch relationship with the EUROCRAN Index (Chapter 6).[6] Also, appearance of the nasolabial profile in children treated in Warsaw and Nijmegen were judged comparable[5] despite a significantly worse anteroposterior dental arch relationship in children from the Warsaw Cleft Centre.[6] Although *cephalometric* versus *dental arch relationship* inconsistency may be explained by a relatively poor ability of cephalometric analysis to discriminate groups regarding the outcome,[20] inconsistent results hinder drawing final conclusions.

Inter-population differences in growth patterns may influence the results of comparisons. Evidence from several investigations of cleft[21] and noncleft[18,22,23] groups suggests that differences between populations of the white race do exist and may affect the reliability of the conclusions in comparative studies. This might have played a significant role in the Warsaw-Nijmegen comparison of dental arch relationship. Because most long-term growth studies were carried out in Western Europe and North America[18,22,23] there is hardly any information regarding facial development in the Slavic ethnic group, to which Poles belong. As some anthropometric data[24] suggest that facial form in the Slavs differs in comparison with individuals with the Anglo-Saxon or Germanic ethnic background (for example, Slavic faces are more brachycephalic), it is likely that craniofacial growth pattern is also different. This is supported by epidemiological evidence, which indicates a higher prevalence of Class II malocclusion in the Netherlands[25] in comparison with Poland.[26] Therefore better dental arch relationship in the Nijmegen group relative to the Warsaw group might have partially resulted from the lesser mandibular prominence observed in the Dutch population.

8.3 Conclusions

While being aware of medium to low quality of the evidence of the retrospective studies of this thesis, the most important conclusions can be summarized as follows:

1. In general, the long-term outcome following the Warsaw one-stage protocol is relatively favorable.
2. The craniofacial morphology in preadolescent children with UCLP who were treated according to the one-stage protocol and alternative multi-stage protocols is comparable.
3. The dental arch relationship following the Warsaw one-stage and Oslo two-stage protocols is comparable.
4. The dental arch relationship following the Warsaw one-stage protocol is less favorable than after Nijmegen three-stage protocol with delayed hard palate closure.
5. The nasolabial appearance following the Warsaw and Nijmegen protocols is comparable.
6. A high skill of the surgeon who operated on all the subjects, might have significantly contributed to the favorable outcome.

8.4 Recommendations for future research

The assessment of treatment outcome in children with UCLP has to be comprehensive, i.e. besides evaluation of facial growth, dental arch relationship, and esthetics, it should include examination of speech, hearing, burden of care, treatment satisfaction, psycho-social development and cost-effectiveness analysis. Most of these aspects should be assessed once the craniofacial growth and orthodontic/orthopedic/orthognathic treatment is complete. Taking this into account, the current investigation should be considered as the first step in comprehensive assessment of the Warsaw protocol. Although the present findings are relatively optimistic and suggest a satisfactory outcome after the one-stage repair of UCLP, final conclusions can only be made after completion of facial growth and treatment.

Considering the methodological problems faced by researchers in the cleft lip and palate field, it is likely that the one-stage repair of UCLP will not be assessed through a RCT study design in the foreseeable future. Therefore, an important question: *How much does the outcome of the Warsaw one-stage protocol depend on the skill of the operator?* will mostly remain unanswered. To some degree, however, this issue can be addressed by comparison of the results achieved by the surgeon who had treated all the patients from the current cohort with the results of two other surgeons performing now one-stage repairs in the Warsaw Cleft Centre.

As mentioned previously, an advent of 3D technology greatly facilitates evaluation of treatment outcome and inter-center comparisons. Therefore, a final evaluation of the outcome of the Warsaw protocol could be enhanced if 3D techniques were used.

8.3 References

1. Fudalej P, Obloj B, Dudkiewicz Z , Hortis-Dzierzbicka M. Mandibular morphology and spatial position following one-stage simultaneous repair of complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2008;45:272-7.
2. Fudalej P, Obłoj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z: Midfacial growth in a consecutive series of preadolescent children with complete unilateral cleft lip and palate following a one-stage simultaneous repair. *Cleft Palate Craniofac J* 2008;45:667-73.

3. Fudalej P, Hortis-Dzierzbicka M, Obłoj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z, Romanowska A. Treatment outcome after one-stage repair in children with complete unilateral cleft lip and palate assessed with the GOSLON yardstick. *Cleft Palate Craniofac J* 2009;46:374-80.
4. Fudalej P, Hortis-Dzierzbicka M, Dudkiewicz Z, Semb G. Dental arch relationship in children with complete unilateral cleft lip and palate following Warsaw (one-stage repair) and Oslo protocols. *Cleft Palate Craniofac J* 2009;46:648-53.
5. Fudalej P, Katsaros C, Bongaarts C, Dudkiewicz Z, Kuijpers-Jagtman AM. Nasolabial esthetics in children with complete unilateral cleft lip and palate after 1- versus 3-stage treatment protocols. *J Oral Max Surg* 2009;67:1661-6.
6. Fudalej P, Katsaros C, Bongaarts C, Dudkiewicz Z, Kuijpers-Jagtman AM. Dental arch relationship in children with complete unilateral cleft lip and palate following one-stage and three-stage surgical protocols. 2010 May 15. [Epub ahead of print]
7. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ* 1996;312:71-2.
8. Centre for Evidence Based Medicine, University of Oxford http://www.cebm.net/index.aspx?o=1025 (accessed 18 September, 2010)
9. U.S. Preventive Services Task Force. http://www.uspreventiveservicestaskforce.org/uspstf08/methods/procmanual4.htm (accessed 18 September, 2010)
10. Farrokhyar F, Karanicolas PJ, Thoma A, Simunovic M, Bhandari M, Devereaux PJ, Anvari M, Adili A, Guyatt G. Randomized controlled trials of surgical interventions. *Ann Surg* 2010;251:409-16.
11. Ergina PL, Cook JA, Blazeby JM, Boutron I, Clavien PA, Reeves BC, Seilor CM. Surgical innovation and evaluation 2. Challenges in evaluating surgical innovation. *Lancet* 2009;374:1097-104.
12. Gelijns AC, Ascheim DD, Parides MK, Kent KC, Moskowitz AJ. Randomized trials in surgery. *Surgery* 2009;145:581-7.
13. Long AF. Outcomes Within Audit: A Process and Outcome Perspective. UK Clearing House on Health Outcomes, *Outcomes Briefing* 1996;7:4–7.
14. Shaw WC, Brattström V, Mølsted K, Prahl-Andersen B, Roberts CT, Semb G. The Eurocleft study: intercenter study of treatment outcome in patients with complete cleft lip and palate. Part 5: discussion and conclusions. *Cleft Palate Craniofac J* 2005;42:93-8.

15. Bearn D, Mildinhall S, Murphy T, Murray JJ, Sell D, Shaw WC, Williams AC, Sandy JR. Cleft lip and palate care in the United Kingdom - the Clinical Standards Advisory Group (CSAG) Study. Part 4: outcome comparisons, training, and conclusions. *Cleft Palate Craniofac J* 2001;38:38-43.
16. Plooij JM, Maal TJ, Haers P, Borstlap WA, Kuijpers-Jagtman AM, Berge SJ. Digital three-dimensional image fusion of the facial soft tissue surface, facial skeleton and dentition in orthodontics and orthognathic surgery. A systematic review. *Int J Oral Maxillofac Surg* (in press).
17. van Vlijmen OJ, Bergé SJ, Swennen GR, Bronkhorst EM, Katsaros C, Kuijpers-Jagtman AM. Comparison of cephalometric radiographs obtained from cone-beam computed tomography scans and conventional radiographs. *J Oral Maxillofac Surg* 2009;67:92-7.
18. El-Batouti A, Øgaard B, Bishara SE, Jakobsen J. Dentofacial changes in Norwegian and Iowan populations between 6 and 18 years of age. *Eur J Orthod* 1995;17:241-9.
19. Nollet PJ, Katsaros C, Huyskens RW, Borstlap WA, Bronkhorst EM, Kuijpers-Jagtman AM. Cephalometric evaluation of long-term craniofacial development in unilateral cleft lip and palate patients treated with delayed hard palate closure. *Int J Oral Maxillofac Surg* 2008; 37:123-30.
20. Shaw WC, Dahl E, Asher-McDade C, Brattström V, Mars M, McWilliam J, Mølsted K, Plint DA, Prahl-Andersen B, Roberts C, The RP. A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 5. General discussion and conclusions. *Cleft Palate Craniofac J* 1992;29:413-8.
21. Daskalogiannakis J, Dijkman GE, Kuijpers-Jagtman AM, Ross RB. Comparison of facial morphology in two populations with complete unilateral cleft lip and palate from two different centers. *Cleft Palate Craniofac J* 2006;43:471-6.
22. Trenouth MJ, Laitung G, Naftel AJ. Differences in cephalometric reference values between five centers: relevance to the Eurocleft Study. *Br J Oral Maxillofac Surg* 1999;37:19-24.
23. Kerr WJ, Ford I. A comparison of facial form in three Western European male groups. *Eur J Orthod* 1986;8:106-11.
24. Klar J. Ethnic differences in facial proportions. In: Farkas LG, Munro IR eds. Anthropometric facial proportions in medicine. Springfield: Charles C Thomas; 1987:19-28.

25. Burgersdijk R, Truin GJ, Frankenmolen F, Kalsbeek H, van 't Hof M, Mulder J. Malocclusion and orthodontic treatment need of 15-74-year-old Dutch adults. *Community Dent Oral Epidemiol* 1991;19:64-7.
26. Śmiech-Słomkowska G. Jakościowa i ilościowa ocean zgryzu wybranej grupy dzieci. *Czas Stomat* 1990;43:704-7.

Chapter 9

Summary

Summary

Chapter 1 is a brief introduction of the subject of cleft lip and palate to the reader. Etiology and epidemiology of the cleft deformity, including Polish epidemiological data, are discussed first. Although the prevalence of cleft lip and palate is relatively low (1 – 2 per 1000 live births), there is a considerable number of children with clefts requiring comprehensive and prolonged treatment worldwide. Complete unilateral cleft lip and palate (UCLP) is one of the most challenging to treat types of the cleft deformity. Facial morphology and treatment strategies in UCLP, including the rationale of employing a 3-stage surgical protocol with delayed hard palate closure as practiced in the Radboud University Nijmegen, are subsequently discussed. Then, the overview and history of a 1-stage simultaneous repair of UCLP is presented. This is followed by a description of the Warsaw approach - a protocol based on 1-stage simultaneous closure practiced in the Warsaw Cleft Centre at the Institute of Mother and Child, Warsaw, Poland. Finally, the methodology of evaluation of treatment outcome in UCLP – single-center versus inter-center research - is explored.

In *Chapter 2* the results of evaluation of midfacial morphology following a 1-stage repair of UCLP are presented. In comparison with non-cleft Polish children, the maxilla in prepubertal subjects with cleft was found shortened, retruded and rotated posteriorly and the maxillary incisors were retroclined. The amount of deviation of midfacial morphology in the 1-stage group was, however, comparable with that found in published reports that examined children with UCLP treated with different methods.

Chapter 3 describes the results of evaluation of mandibular morphology and spatial position following 1-stage simultaneous repair of UCLP. The mandible in prepubertal children was found to be retruded and at a larger inclination to the cranial base as compared with controls. Both total mandibular length and length of the mandibular body were smaller by 2 mm than in the control group, whereas height of the ramus and gonial angle were similar in both groups. It was concluded, however, that, as was the case with midfacial morphology, the amount of deviation

in the 1-stage group was comparable with that found in other published reports.

In *Chapter 4* the results of within-the-center evaluation of dental arch relationship in a sample of 28 consecutive cases are presented. Two examiners rated the dental arch relationship with the GOSLON Yardstick on the basis of photographs. It was found that 57% of patients were assigned the GOSLON 1 or 2 categories (very good and good outcome), 32% were rated 3 (average outcome), and 11% were rated 4 or 5 (poor and very poor outcome). It was concluded that dental arch relationship following one-stage repair was comparable with the results of other centers with a favorable treatment outcome.

The results of the Warsaw-Oslo inter-center comparison of dental arch relationship are presented in *Chapter 5*. The dental models of two samples of 61 consecutively treated patients, matched regarding age and gender, were evaluated with the GOSLON Yardstick by a panel consisting of 4 examiners. The study models were given random numbers to blind their origin. The intra- and inter-rater agreement was high. No difference in dental arch relationship between Warsaw and Oslo groups was found (mean GOSLON score = 2.68 and 2.65 for Warsaw and Oslo samples, respectively). The distribution of the Goslon grades was similar in both groups. It was concluded that the dental arch relationship following 1-stage repair (Warsaw protocol) was comparable with the outcome of the Oslo Cleft Team's protocol.

The results of the Warsaw-Nijmegen inter-center comparison of dental arch relationship are described in *Chapter 6*. The dental casts of 61 consecutively treated children were assigned random numbers to blind their origin. 4 raters graded dental arch relationship and palatal morphology using the EUROCRAN Index. The intra- and inter-rater agreement was moderate to very good. Dental arch relationship in the Warsaw 1-stage sample was less favorable than in Nijmegen 3-stage group (mean scores 2.58 and 1.97 for 1-stage and 3-stage samples, respectively; $p < 0.000$). Palatal morphology in the 1-stage sample was more favorable than in the 3-stage group (mean scores 1.79 and 1.96 for 1-stage and 3-stage samples, respectively; $p = 0.047$). It was concluded that the dental arch relationship following 1-stage repair (Warsaw protocol) was less favorable than that following a 3-stage protocol, whereas the palatal morphology in the Warsaw sample was more favorable than in the Nijmegen sample.

Chapter 7 describes nasolabial esthetics after a 1-stage (Warsaw group, 41 boys and 19 girls) or a 3-stage (Nijmegen group, 30 boys and 18 girls) treatment protocol. 4 components of the nasolabial appearance: nasal form, nasal deviation, mucocutaneous junction, and profile view were assessed by 4 raters with the aid of a 5-grade esthetic index of Asher-McDade. Nasal form was judged as the least esthetic in both groups and graded 3.1 (SD = 1.1) and 3.2 (SD = 1.1). Nasal deviation, mucocutaneous junction, and profile view were scored from 2.1 (SD = 0.8) to 2.3 (SD = 1.0) in both groups. Treatment outcome following the Nijmegen and Warsaw protocols was comparable. Neither overall, nor any of the 4 components of the nasolabial appearance showed inter-center difference ($p > 0.1$). It was concluded that the nasolabial appearance following the Warsaw and Nijmegen protocols was comparable.

Finally, in *Chapter 8*, a general discussion of the methodological problems encountered during this investigation is presented. The overall outcome of the Warsaw protocol is also critically discussed and limitations of this study – emphasized. This chapter ends with suggestions for further research, particularly an evaluation of speech and a final assessment of the outcome once craniofacial growth is complete.

Chapter 10

Samenvatting

In *Hoofdstuk 1* wordt een korte inleiding gegeven over schisis. De etiologie en epidemiologie van schisis, waaronder de Poolse epidemiologische gegevens omtrent schisis worden beschreven. De prevalentie van schisis is met 1-2 baby's op 1000 niet hoog. Deze kinderen vragen echter wel een lange gecompliceerde multidisciplinaire behandeling. Een unilaterale cheilognathopalatoschisis (UCLP) is een van de meest uitdagende en gecompliceerde schisisafwijkingen om goed te behandelen. Protocollen voor behandeling verschillen. Gelaatsmorfologie en behandelstrategieën voor unilaterale schisis worden besproken waaronder de rationale voor het sluiten van het gehemelte in 3 stappen met een late sluiting van het harde gehemelte zoals dit in Nijmegen wordt toegepast. een korte geschiedenis en overzicht wordt hierna gegeven van een ander behandelprotocol waarbij het gehemelte gelijktijdig in 1 keer wordt gesloten. Hierna volgt een omschrijving van het protocol dat door het schisisteam in het Institute of Mother and Child in Warschau wordt toegepast. Dit protocol is gebaseerd op het gelijktijdig sluiten van het gehele gehemelte. Aan het einde van het hoofdstuk wordt de methodologie van het meten van het behandelingsresultaat voor UCLP in singlecentre en intercentre onderzoek besproken.

In *hoofdstuk 2* worden de resultaten van de morfologie van het middengezicht na een 1-fase sluiting van het gehemelte besproken. De patiënten werden vergelijken met Poolse kinderen zonder schisis. In vergelijking met deze controlegroep vertoonden prepuberale UCLP patiënten een kortere, retrusieve maxilla die naar posterior geroteerd was met retroclinatie van de incisieven. De mate van afwijkende morfologie van het middengezicht in de 1-fase groep was echter vergelijkbaar met de onderzoeksresultaten uit andere gepubliceerde onderzoeken over kinderen met een UCLP maar behandeld volgens een ander protocol.

De resultaten voor de positie en morfologie van de mandibula na een 1-fase gehemeltesluiting worden beschreven in *hoofdstuk 3*. In vergelijking met de controlegroep hadden prepuberale kinderen met een UCLP na de behandeling een retrusieve mandibula met een grotere inclinatie in relatie tot de craniale basis. De totale lengte van de mandibula alsmede de lengte van het corpus mandibulae waren 2 mm korter dan die van de controlegroep. De hoogte van de ramus en de grootte van de gonionhoek waren gelijk tussen beide groepen. Deze resultaten kwamen, net zoals de morfologie van het middengezicht, overeen met andere gepubliceerde onderzoeken.

Hoofdstuk 4 laat de resultaten van het schisiscentrum in Warschau zien voor de relatie van de tandbogen van 28 patiënten. Twee onderzoekers scoorden de tandboogrelatie met de GOSLON yardstick aan de hand van foto's. 57% van de patiënten vielen in de GOSLON categorieën 1 en 2 (wat een zeer goed tot goed resultaat betekent), 32% scoorden categorie 3 (gemiddeld resultaat) en 11% scoorden categorieën 4 en 5 (slecht tot zeer slecht resultaat). Geconcludeerd kon worden dat de relatie tussen beide tandbogen na een 1-fase sluiting van het gehemelte een vergelijkbaar resultaat gaf als in andere centra met goede behandelresultaten.

De resultaten van de vergelijking van de occlusie tussen de schisiscentra van Warschau en Oslo worden beschreven in *hoofdstuk 5*. De gipsmodellen van twee groepen van 61 behandelde patiënten, gematched voor leeftijd en geslacht, werden beoordeeld met de GOSLON Yardstick door een panel van vier onderzoekers. De modellen werden gerandomiseerd met nummers zodat het land waar de patiënt behandeld was niet bekend was. De intra- en interobserver betrouwbaarheid was hoog. Er werden geen verschillen gevonden in tandboogrelatie tussen de groepen van Warschau en Oslo (de gemiddelde GOSLON score was voor de Warschau en Oslo groepen respectievelijk 2.68 en 2.65). De verdeling van de GOSLON categorieën was gelijk in beide groepen. Geconcludeerd werd dat de relatie van de tandbogen na 1-fase sluiting (het Warschau protocol) vergelijkbaar is met het behandelresultaat van het schisisteam uit Oslo.

In *hoofdstuk 6* worden de resultaten van een vergelijking van de relatie van de tandbogen tussen de schisiscentra in Nijmegen en Warschau besproken. De gipsmodellen van twee groepen van 61 behandelde patiënten werden geanonimiseerd zodat het land waar de patiënt behandeld was niet bekend was. Vier onderzoekers scoorden de tandboogrelatie en de morfologie van het gehemelte aan de hand van de EUROCRAN index. De intra- en interobserver betrouwbaarheid was gemiddeld tot zeer goed. De occlusie van de groep met het 1-fase protocol uit Warschau was minder goed dan de groep met het 3-fase protocol uit Nijmegen (respectievelijke score 2.58 en 1.97; $p < 0.000$). De morfologie van het gehemelte na de 1-fase behandeling was beter dan die na de 3-fase behandeling (gemiddelde score respectievelijk 1.79 en 1.96; $p = 0.047$). De relatie van de tandbogen is na de 1-fase behandeling van het Warschau team minder goed dan na de 3-fase sluiting van het team in Nijmegen. De morfologie van het gehemelte laat het omgekeerde resultaat zien.

Hoofdstuk 7 beschrijft de resultaten voor de esthetiek van neus en bovenlip na een 1-fase sluiting (de Warschau groep, 41 jongens en 19 meisjes) en na de 3-fase sluiting van het gehemelte (de Nijmegen groep, 30 jongens en 18 meisjes). Vier onderdelen van de nasolabiale esthetiek werden gescoord, te weten: vorm van de neus, deviatie van de neus, verloop van het lippenrood, en het neusprofiel. Deze werden gescoord door vier onderzoekers met hulp van de 5-puntsschaal voor nasolabiale esthetiek bij schisispatiënten van Asher-Mc Dade. De vorm van de neus scoorde het slechtst in beide groepen, 3.1 (SD = 1.1) en 3.2 (SD = 1.1). De deviatie van de neus, verloop van het lippenrood en het neusprofiel hadden scores van 2.1 (SD = 0.8) tot 2.3 (SD =1.0) in beide groepen. Het behandelresultaat was voor de Nijmegen en Warschau protocollen vergelijkbaar. De al gehele esthetiek van de neus, dan wel de vier apart gescoorde onderdelen, lieten geen verschil tussen de centra zien (p =0.1). Geconcludeerd werd dat de esthetiek van lip en neus na behandeling met het Warschau of Nijmegen protocol vergelijkbaar was.

Hoofdstuk 8 geeft een discussie over de methodologische problemen die tijdens het onderzoek aan het licht kwamen. Het algehele behandelresultaat van het Warschau protocol wordt kritisch beschouwd en beperkingen van het onderzoek worden benadrukt. Het hoofdstuk eindigt met suggesties voor verder onderzoek, vooral met betrekking tot spraak en een uiteindelijke evaluatie van de behandeling nadat de craniofaciale groei beëindigd is.

I dedicate this study to all Polish children with a cleft lip and palate - I wish them to receive the best available treatment.

I would like to express my deepest gratitude to two wonderful persons without whom this study would not have been possible: Prof. Anne Marie Kuijpers-Jagtman and Prof. Zofia Dudkiewicz.

My special thanks to all members of the Warsaw Cleft Team from the Institute of Mother and Child. Your help was invaluable.

Prof. Gunvor Semb and Prof. Christos Katsaros – thank you for inspiration and support.

I would also like to thank all persons from the Department of Orthodontics and Craniofacial Biology of the Radboud University Nijmegen Medical Centre for making my first months in Nijmegen so splendid.

Mette, I am very grateful for your translations.

Dit proefschrift draag ik op aan alle Poolse kinderen met een schisis. Ik spreek de wens uit dat zij de best mogelijke zorg kunnen krijgen.

Graag wil ik mijn welgemeende dank uitspreken naar de twee personen zonder wie dit proefschrift niet tot stand zou zijn gekomen: Prof. Anne Marie Kuijpers-Jagtman en Prof. Zofia Dudkiewicz.

In het bijzonder wil ik alle medewerkers van het Schisisteam van het Instituut voor Moeder en Kind bedanken. Jullie hulp was van grote waarde.

Verder wil ik Prof. Gunvor Semb en Prof. Christos Katsaros bedanken voor hun inspiratie en ondersteuning.

Als laatste wil ik iedereen van de Vakgroep Orthodontie en Craniofaciale Biologie van het St Radboud Universitair Medisch Centrum Nijmegen bedanken voor de warme en aangename eerste maanden in Nijmegen.

Mette, bedankt voor je vertaling.

Pracę tę dedykuję wszystkim polskim pacjentom z rozszczepem wargi i podniebienia życząc im, aby byli leczeni w najlepszy dostępny sposób.

Chciałbym wyrazić swoją głeboką wdzięczność dwóm cudownym osobom, bez których ta praca nigdy by nie powstała: prof. Anne Marie Kuijpers-Jagtman oraz prof. Zofii Dudkiewicz.

Wszystkim członkom zespołu rozszczepowego z Instytutu Matki i Dziecka dziekuję za bezcenną pomoc.

Serdecznie dziękuję również prof. Gunvor Semb oraz prof. Christosowi Katsaros za inspirację i wsparcie.

Dziękuję gorąco wszystkim moim koleżankom i kolegom z Centrum Medycznego Uniwersytetu Radboud w Nijmegen za wspaniałe pierwsze miesiące mojej pracy.

Mette, jestem Ci bardzo wdzięczny za tłumaczenia.

Piotr Fudalej was born on 14 January 1968 in Sosnowiec in southern Poland. He obtained his high-school diploma in 1986 in Walbrzych, Poland. In the same year, 1986, he won a 1st prize in a nation-wide contest in biology. Piotr graduated from the Warsaw Medical University in 1991 and, from 1990 to1992, he also studied biology at the Warsaw University.

Piotr always wished to learn. Following this desire, he completed his postgraduate training in orthodontics at the University of Washington, Seattle, USA, in 1998. In fact, he was the first dentist in the post-war history of Poland who obtained a certificate of specialist in orthodontics as well as a Master of Science in Dentistry degree from an American university. In 1999 he defended with highest honors his doctoral thesis entitled “Effects of postadolescent mandibular rotation on stability of incisal alignment” at the Lublin Medical University.

His interests in research in the cleft lip and palate field started in 2004 when he joined the Cleft Team at the Warsaw Institute of Mother and Child, Poland. Working in this busy cleft center, he started evaluation of the outcome of one-stage surgical repair of unilateral cleft lip and palate, a rather unique method of treatment of children with cleft.

Since the 1st of December 2010 he joined the faculty at the Department of Orthodontics and Craniofacial Biology at the Radboud University Nijmegen Medical Centre Dental department. He is a member of the editorial board of the “European Journal of Orthodontics” and “Ortodoncie” (the official journal of the Czech Orthodontic Society). He is a recipient of the 2010 Samuel Berkowitz Award for the article “Dental Arch Relationship in Children With Complete Unilateral Cleft Lip and Palate Following Warsaw (One-Stage Repair) and Oslo Protocols”, which is part of his PhD thesis (chapter 5). This award is given yearly by the Cleft Palate Foundation for the best long-term outcomes study published in the Cleft Palate-Craniofacial Journal.

Piotr has maintained a private practice limited to orthodontics in Warsaw since 1998. He is married and has five children aged from 3 to 8 (5-year-old triplets among them).

Publications

In international journals:

1. Fudalej P, Årtun J. Mandibular growth rotation effects on post-retention stability of mandibular incisor alignment. *Angle Orthod* 2007;77:199-205.
2. Fudalej P, Kokich V, Leroux B. Determining the cessation of vertical growth of craniofacial structures to facilitate placement of single-tooth implants. Am J Orthod Dentofacial Orthop *Am J Orthod Dentofacial Orthop* 2007;131(4 Suppl):S59-67.
3. Obloj B, Fudalej P, Dudkiewicz Z. Cephalometric standards of Polish 10-year-olds with normal occlusion. *Angle Orthod* 2008;78:262-9.
4. Fudalej P. Long-term changes of the upper lip position relative to incisal edge. *Am J Orthod Dentofacial Orthop* 2008;133:204-9.
5. Fudalej P, Obloj B, Dudkiewicz Z, Hortis-Dzierzbicka M. Mandibular morphology and spatial position following one-stage simultaneous repair of the complete unilateral cleft lip and palate. *Cleft Palate Craniofac J* 2008;45:272-7.
6. Fudalej P, Rothe L, Bollen A-M. Effects of post-treatment growth potential, as measured with CVM method, on relapse of incisor alignment. *Am J Orthod Dentofacial Orthop* 2008;134:238-44.
7. Fudalej P. Is post-adolescent anterior mandibular growth rotation a risk factor of incisor relapse in males? *Am J Orthod Dentofacial Orthop* 2008;134:245-50.
8. Fudalej P, Obloj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z. Midfacial growth in a consecutive series of preadolescent children with complete unilateral cleft lip and palate following a one-stage simultaneous repair. *Cleft Palate Craniofac J* 2008;45:667-73.
9. Fudalej P, Hortis-Dzierzbicka M, Obloj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z. Treatment outcome after one-stage repair in children with complete unilateral cleft lip and palate assessed with the GOSLON yardstick. *Cleft Palate Craniofac J* 2009;46:374-80.
10. Fudalej P, Katsaros C, Bongaarts C, Dudkiewicz Z, Kuijpers-Jagtman AM. Nasolabial appearance in UCLP following two surgical protocols. *J Oral Max Surg* 2009;67:1661-6.

11. Fudalej P, Hortis-Dzierzbicka M, Dudkiewicz Z, Semb G. Comparison of dental arch relationship in children with unilateral cleft lip and palate following Warsaw (one-stage simultaneous repair) and Oslo protocols. Cleft *Palate Craniofac J* 2009;46:648-53.
12. Fudalej P, Bollen A-M. Effectiveness of the Cervical Vertebral Maturation method to predict post-peak circumpubertal growth of the craniofacial structures. *Am J Orthod Dentofacial Orthop* 2010;137:59-65.
13. Fudalej P, Dragan M, Wedrychowska-Szulc B. Prediction of the outcome of orthodontic treatment of Class III malocclusion - a systematic review. *Eur J Orthod* 2010 Jul 22. [Epub ahead of print].
14. Fudalej P, Katsaros C, Bongaarts C, Dudkiewicz Z, Kuijpers-Jagtman AM. Dental arch relationship in children with complete unilateral cleft lip and palate following 1- vs. 3-stage treatment protocols. *Clin Oral Investig* 2010 May 15. [Epub ahead of print].
15. Fudalej P, Bollen A-M, Hujoel IA. Relapse of mandibular incisor alignment is not associated with total mandibular rotation. *Am J Orthod Dentofacial Orthop* 2010;138:392.e1-7.
16. Fudalej P, Surowiec Z, Offert B, Dudkiewicz Z, Katsaros C. Craniofacial morphology in complete unilateral cleft lip and palate patients consecutively treated with one-stage repair of the cleft. *J Craniofac Surg* 2010;21:1468-73.
17. Fudalej P, Antosiewicz J. Are orthodontic distalizers reinforced with the temporary skeletal anchorage devices (TSADs) effective? A systematic review. *Am J Orthod Dentofacial Orthop* (accepted for publication).
18. Fudalej P, Janiszewska-Olszowska J, Wedrychowska-Szulc B, Katsaros C. Early bone-grafting has a negative effect on dimensions of the maxillary dental arch of pre-school children with CUCLP. *Orthod Craniofac Res* (accepted for publication)

Books:

Fudalej P. Wynik leczenia rozszczepu wargi i podniebienia metodą jednoczasową – porównanie między ośrodkami. [Outcome of treament of unilateral cleft lip and palate – inter-centre study] in Polish: Lublin, Bestprint, 2009.

In Polish journals:

1. Fudalej P. Chirurgiczno-ortodontyczne leczenie dorosłego pacjenta ze zgryzem otwartym przednim i stłoczeniami w obu łukach zębowych. *Stomatologia Współczesna* 1998;5:359-65.
2. Fudalej P. Wrodzony brak siekacza górnego – wybór metody leczenia. *Ortodoncja Współczesna* 2003;5(3):64-70.
3. Fudalej P. Ocena skuteczności prognozowania rotacji żuchwy na podstawie piśmiennictwa. *Ortodoncja Współczesna* 2004;2(22):44-9.
4. Fudalej P, Obłoj B, Dudkiewicz Z. Odległa analiza szerokości i długości górnego łuku zębowego u osób z jednostronnym rozszczepem wargi i podniebienia. *Medycyna Wieku Rozwojowego* 2005;9:781-9.
5. Fudalej P, Obłoj B, Dudkiewicz Z. Budowa i położenie żuchwy u osób z całkowitym jednostronnym rozszczepem wargi i podniebienia leczonych metodą jednoetapową. *Medycyna Wieku Rozwojowego* 2006;10:875-84.
6. Fudalej P, Obłoj B, Dudkiewicz Z. Budowa twarzoczaszki 10-latków z jednostronnym całkowitym rozszczepem wargi i podniebienia leczonych metodą jednoczasową. *Medycyna Wieku Rozwojowego* 2007;11:45-50.
7. Fudalej P, Król Z, Dudkiewicz Z. Cefalometryczna ocena symetrii twarzoczaszki osób z jednostronnym całkowitym rozszczepem wargi i podniebienia leczonych metodą jednoczasową. *Medycyna Wieku Rozwojowego* 2007;11:255-9.
8. Fudalej P, Obłoj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z. Cefalometryczna ocena budowy twarzoczaszki dzieci przed okresem pokwitania z jednostronnym rozszczepem podniebienia pierwotnego. *Medycyna Wieku Rozwojowego* 2007;11:247-53.
9. Fudalej P. Wybrane metody leczenia ortodontycznego doprzednich wad zgryzu. *Magazyn Stomatologiczny* 2007;17(11):20-4.
10. Fudalej P, Chrostowska E, Maciejewska A. Próba oceny metody Nolli oraz Demirjiana do określania indywidualnego wieku zębowego dzieci z prawidłową budową części twarzowej czaszki. *Czasopismo Stomatologiczne* 2007;60:741-1.
11. Fudalej P. Rokowanie dotyczące skuteczności ortodontycznego leczenia wad doprzednich – przegląd piśmiennictwa. *Czasopismo Stomatologiczne* 2007;60:806-4.

12. Fudalej P, Obłoj B, Miller-Drabikowska B, Samarcew-Krawczak A, Dudkiewicz Z. Porównanie budowy części twarzowej czaszki u dzieci przed okresem pokwitania z różnymi formami jednostronnego rozszczepu podniebienia pierwotnego oraz wtórnego. *Czasopismo Stomatologiczne* 2008;61:118-24.